CORLAS 2024

VIENNA

Annual Meeting

Collegium Oto-Rhino-Laryngologicum
Amicitiae Sacrum

26.08.2024 – 28.08.2024
Hotel Palais Hansen
Vienna, Austria

NUCALA
mepolizumab

GSK

Breathe in. Breathe out. Nucala.

The only anti-IL-5 therapy approved to treat nasal polyps.[1]

Significantly improves quality of life for patients with CRSwNP[2]

Established safety profile, similar to placebo[2]

Simple dosing, once a month[1]

NUCALA'S TARGETED ANTI-IL-5 MECHANISM OF ACTION TACKLES NASAL POLYPS AT THE ROOT OF THE PROBLEM. MEPOLIZUMAB REGULATES TYPE 2 INFLAMMATION BY INHIBITING IL-5 AND THUS REDUCING EOSINOPHILS IN THE BLOOD TO PHYSIOLOGICAL LEVELS. [1 – 6]

1. Nucala Fachinformation, aktueller Stand. **2.** Han J K, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, doubleblind, placebo-controlled, phase 3 trial. The Lancet Respiratory Medicine, 2021; 9(10), 1141-1153. **3.** Stoop AE, et al. Eosinophils in nasal polyps and nasal mucosa: an immunhistochemical study. Journal of allergy and clinical immunology, 1993; 91(2), 616-622. **4.** Tosun F et al. Relationship between postoperative recurrence rate and eosinophil density of nasal polyps. Annals of Otology, Rhinology & Laryngology, 2010; 119(7), 455-459. **5.** Fujieda S, et al. Eosinophilic chronic rhinosinusitis. Allergology international. 2019; 68(4), 403-412. **6.** Lou H, et al. Cellular phenotyping of chronic rhinosinusitis with nasal polyps. Rhinology, 2016; 54(2), 150-159.

The prescribing information can be found on page 192 | PM-AT-MPL-JRNA-240006 | 06/2024

CORLAS 2024 VIENNA

Vienna welcomes CORLAS – the Collegium !
Dear CORLAS members, dear guests and friends !

It is an outstanding honor to host the 2024 Annual Meeting of
the Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum in Vienna !

Since the Collegiums founding in 1926, it is now after Gustav Hofer from Graz (meeting 1959 in Vienna) and Klaus Albegger (meeting 1995 in Salzburg), the 3rd time that CORLAS takes place in Austria.
For the very first time in 98 years, the CORLAS president is from Vienna, the worlds oldest and first Otology ENT University department, founded in 1873 by Adam Politzer. For myself this is an unbelievable extraordinary honor, the highlight of my academic, clinical and scientific career and also a sign of international acknowledgement and appreciation reflecting the excellent relations in our international scientific ENT/ORL community.
We tried to establish a wonderful program for You in all aspects of science, cultural backgrund, culture, food and Viennese hospitality. Each item of the agenda was tested personally and carefully selected. Sundays family tour into the „Wachau“ will give You a glimpse of the Danube and countryside Austria. The Cultural Evening in the Golden Hall of the Wiener Musikverein and the Heurigen where Ludwig van Beethoven wrote his Heiligenstädter Testimonial are some unsurpassable highlights, as well as our members and accompanying persons dinner in the cupula of the Museae of Natural History and Fine Arts. Not to forget the historic Vienna Townhall which will be our scenery for the Gala Evening.
Scientifically we will see the outmost recent research topics in our field. Especially covering the topics of robotics in otology, latest gene-therapy and molecularbiology research in hearing disorders, as well as new tumormarkers, immunotherapy and antiallergic treatment through most recent biologica and the immunological background.
The historic Palais Hansen will give us a worthy and nice environment for prosperous and fruitfull scientific sessions and dicussions.

We invite all of You to come and join. Vienna and us is awaiting You !

Sincerely Yours


Wolf-Dieter Baumgartner
(President)


Peter Franz
(Vice-President)


Alexandra Jappel
(Congress Secretary)

CORLAS Board at the 2024 Vienna Meeting

Board

President	**Wolf-Dieter Baumgartner**	Vienna
Vice President	**Peter Franz**	Vienna
General Secretary	**Antti Mäkitie**	Helsinki
Second Secretary	**D. Bradley Welling**	Boston
Treasurer	**Sandro Stöckli**	St. Gallen
Councillor	**Barbara Wollenberg**	Munich
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Councillor	**Kaoru Ogawa**	Tokyo
Editorial Secretary	**Matti Anniko**	Stockholm
Past President	**Tatsuya Yamasoba**	Tokyo

Credentials Committee / International Jury

Chair	**Allen Ryan**	San Diego
	Rene Leémans	Amsterdam
	Valerie Lund	London

Founders

C.E. Benjamins
A.P.H.A. de Kleyn

Presidents

1926	H. Zwaardemaker	Groningen / The Netherlands	(founding meeting)
1927	F.R. Nager	Zurich / Switzerland	
1928	F. Schmiegelow	Copenhagen / Denmark	(business meeting)
1929	A.A. Gray	London / Great Britain	
1930	C. Voss	Frankfurt am Main / Germany	
1931	G. Portmann	Bordeaux / France	
1932	A.G. Tapia	Madrid / Spain	(business meeting)
1933	A. Precechtel	Prague / Czech Republic	
1934	G. Holmgren	Stockholm / Sweden	
1935	A. Rejto	Budapest / Hungary	
1937	F. Brunetti	Venice / Italy	
1938	A. de Kleyn	Groningen / The Netherlands	
1947	C. Hicquet	Brussels / Belgium	(informal meeting)
1948	N.Rh. Blegvad	Copenhagen / Denmark	(informal meeting)
1949	N.Rh. Blegvad	London / Great Britain	(buisness meeting)
1950	G. Ferreri	Rome / Italy	(informal meeting)
1951	Y. Meurman	Helsinki / Finland	(business meeting)
1952	L. Ruedi	Zurich / Switzerland	
1953	L. Ruedi	Amsterdam / T. Netherlands	(business meeting)
1954	V.E. Negus	London / Great Britain	
1955	B. Gusic	Zagreb-Belgrade / Yugoslavia	
1956	G. Portmann	Bordeaux / France	
1957	G. Portmann	Washington / USA	(business meeting)
1958	G.T. Wilson	Dublin / Ireland	
1959	G. Hofer	Vienna / Austria	
1960	M. Arslan	Padua / Italy	
1961	M. Arslan	Paris / France	(business meeting)
1962	J. Chryssikos	Athen / Greece	
1963	I. Simson Hall	Edinburgh / Great Britain	
1964	H. Wullstein	Würzburg / Germany	
1965	H. Wullstein	Tokyo / Japan	(business meeting)
1966	P. Mounier-Kuhn	Lyon / France	
1967	J. Lindsay	Chicago / USA	
1968	T. Leegard	Oslo / Norway	
1969	T. Leegard	Mexico City / Mexico	(business meeting)
1970	E. Borghesan	Palermo / Italy	
1971	W.H. Struben	Rotterdam / The Netherlands	
1972	E. Escher	Berne / Switzerland	
1973	E. Escher	Venice / Italy	(business meeting)

1974	J. Angell James	Bristol / Great Britain	
1975	I.F. Padovan	Dubrovnik / Croatia	
1976	C.A. Hamberger	Stockholm / Sweden	
1977	C.A. Hamberger	Buenos Aires / Argentina	(business meeting)
1978	M. Ciges	Granada / Spain	
1979	L. Surjan	Budapest / Hungary	
1980	F.A. Sooy	San Francisco / USA	
1981	F.A. Sooy	Budapest / Hungary	(lunch meeting)
1982	L.B.W. Jongkees	The Hague / The Netherlands	
1983	P. Pialoux	Paris / France	
1984	L.S. Manolidis	Corfu / Greece	
1985	A. Coyas	Miami / USA	(lunch meeting)
1986	H.H. Naumann	Munich / Germany	
1987	G. Rossi	Turin / Italy	
1988	I. Watanabe	Tokyo / Japan	
1989	I. Watanabe	Madrid / Spain	(lunch meeting)
1990	C.R. Pfaltz	Basel / Switzerland	
1991	D.F.N. Harrison	York / Great Britain	
1992	M.N. Kotby	Cairo / Egypt	
1993	M.N. Kotby	Istanbul / Turkey	(lunch meeting)
1994	M. Andrea	Estoril / Portugal	
1995	K. Albegger	Salzburg / Austria	
1996	P.W. Alberti	Vancouver / Canada	
1997	P.W. Alberti	Sydney / Australia	(lunch meeting)
1998	P. Bretlau	Copenhagen / Denmark	
1999	A. Morgan	Lyon / France	
2000	J.B. Snow	Washington / USA	
2001	J.B. Snow	postponed	
2002	P. van den Broek	Noordwijk / The Netherlands	
		Cairo / Egypt	(lunch meeting)
2003	R. Grénman	Helsinki / Finland	
2004	P. Mangabeira Albernaz	Salvador / Brazil	
2005	P. Mangabeira	Rome / Italy	(lunch meeting)
2006	G. Tavartkiladze	Moscow / Russia	
2007	C.S. Kim	Seoul / Korea	
2008	H. Scherer	Berlin / Germany	
2009	H. Scherer	Sao Paolo / Brazil	(lunch meeting)
2010	I. Sziklai	Budapest / Hungary	
2011	P. Lefebvre	Bruges / Belgium	
2012	R. Filipo	Rome / Italy	
2013	M. Önerci	Seoul / Korea	(lunch meeting)
2014	M. Önerci	Istanbul / Turkey	

2015	P.A. Wackym	San Francisco / USA	
2016	R. Dauman	Bordeaux / France	
2017	O. Sterkers	Paris / France	(lunch meeting)
2018	W.N. Huang	Beijing / China	
2019	M. Kompis	Berne / Switzerland	
2020	M. Goycoolea	Pandemic – Virtual business meeting	
2021	M. Goycoolea	Pandemic – Virtual business meeting	
2022	M. Goycoolea	Santiago / Chile	
2023	T. Yamasoba	Tokyo / Japan	

General Secretaries

1926 - 1940	**C.E. Benjamins**	Groningen
1940 – 1960	**E. Huizinga**	Groningen
1960 – 1976	**L.B.W. Jongkees**	Amsterdam
1977 – 1986	**C.R. Pfaltz**	Basel
1987 - 2000	**P. van den Broek**	Nijmegen
2000 - 2008	**P. Karma**	Helsinki
2008 - 2015	**R. Dauman**	Bordeaux
Since 2015	**A. Mäkitie**	Helsinki

Treasurers

1926 - 1936	**A.R. Tweedie**	Nottingham
1936 – 1950	**V.E. Negus**	London
1950 – 1966	**L. Ruedi**	Zurich
1966 – 1990	**M. Portmann**	Bordeaux
1990 - 1999	**J.M. Aran**	Bordeaux
2000 - 2008	**R. Dauman**	Bordeaux
2008 - 2015	**R. Grénman**	Turku
Since 2016	**S. Stöckli**	St. Gallen

Congress Information

Meeting Venue

Palais Hansen
Schottenring 24
A – 1010 Wien
www.anantara.com/en/palais-hansen-vienna
palaishansen@anantara-hotels.com

Language

The official language of the Congress will be ENGLISH.

Information

Our staff at the registration desk will be happy to assist you with any questions or issues.

Opening hours of the registration desk

You get the meeting materials at the registration desk.
The registration desk is located on the ground floor of the Hotel Palais Hansen infront of hall “Theophil” and is open at the following hours:

Saturday, August 24th	15:00 – 17:00
Sunday, August 25th	15:00 – 20:00
Monday, August 26th	07:30 – 16:00
Tuesday, August 27th	07:30 – 17:00
Wednesday, August 28th	07:30 – 17:00

Opening hours exhibition

Monday, August 26th – Wednesday 28th	08:00 – 17:00

Name Badges

You will receive a personalized badge when collecting Your registration documents. This badge must be clearly visible at all times during the Congress and grants access to the Scientific Sessions and the Commercial Exhibition. You also should wear it at all social events to be identified participant of CORLAS 2024.

Certificate of Attendance

An Attendance Certificate will be included in the Congress bag for official participants to the congress.

Official CORLAS Group Photo

The official CORLAS group photo will be taken on August 27th during the Member`s Dinner at the Natural History Museum. Meeting point: Museum INSIDE staircase around 19:45 !

Lunches and Coffee Breaks

Coffee breaks and Lunch buffet are included in the registration fee. Coffee as well as Lunch will be served in the exhibition area and hotel restaurant.

Transport City Centre of Vienna (72 h Ticket "Wiener Linien")

You will receive a 72 hours ticket "Wiener Linien" when collecting Your registration documents. The ticket offers you free travel on Vienna's public transport for 72 hours from validation. It is valid on all public transport services in the core zone of Vienna.

Don't forget to validate your ticket!
If you are travelling with a paper ticket, you need to stamp it in order to validate it in the blue ticket stampers before boarding. You find the blue ticket stampers onboard of trams and busses and at the barriers before entering the underground railway.
We kindly ask to bring your “Wiener Linien” ticket with you for all social events in Vienna.

Unforseen events or program changes

Due to unforeseen or external factors, the program may be changed in some extent. The participant acknowledges that he / she has no rights to lodge damage claims against the organizers, should the holding of the meeting be hindered or prevented by unexpected political, health or economic events or generally by force majeure, or should the non-appearance of speakers or other reasons necessitate program changes. Participants take part in all events of this meeting at their own risk. With his / her registration the participant acceps this proviso.

Insurance

Participants are advised to arrange their own personal travel insurance (health and accident insurance) prior to travelling to the Congress.
The Congress Organisers will not assume any responsibility for accidents, losses or damages to property and persons, as well as for delays or modification in the programme, caused by unforeseen circumstances.

Information for Oral Presentation

All presentations are to be done digitally.
Please submit your presentation material at the Speaker`s Ready Room on the first floor at least 1 hour prior to your session.

Please make your presentation on a Windows Power-Point or Macintosh Power-Point and save the data on a USB flash drive.
The presentation time is stated in the program.
Presenters are required to keep presentation within the time limit.
Chairs are required to remain within the time allotted for the session and each presentation.

SOCIAL PROGRAM

Sunday, 25TH August 2024

Welcome Reception in Palais Hansen

Start: 19:00 Meet & Greet
Conference President´s Welcome, flying buffet and live music
End: 23:30
Dress Code: Casual

Monday, 26TH August 2024

Cultural Evening

Special Performance in Goldener Saal des Viennna Musikverein

Transfer 16:00 from Hotel Palais Hansen
Start of performance 17:00
www.musikverein.at
After the concert transfer to Heurigen “Mayer am Pfarrplatz”
www.pfarrplatz.at
End 23:30 / 24:00 (Transfer back to Palais Hansen from 22:30 until 24:00 – bus shuttle)
Dress Code: Business Casual

Tuesday, 27TH August 2024

Member´s Dinner at the "Naturhistorisches Museum Wien" and Accompanying´s Dinner at the "Kunsthistorisches Museum Wien"

Start 19:00
CORLAS GROUP PHOTO – 19:45 at stairway
Cocktail & guided tour, seated Gala Dinner
Live Music
End around 23:00 / 23:30
Dress Code: Formal

Members: **NATURHISTORISCHES MUSEUM** www.nhm-wien.ac.at
Accompanying: **KUNSTHISTORISCHES MUSEUM** www.khm.at

Wednesday, 28TH August 2024

Gala Dinner in the historic festival hall at town hall

Start 19:00
Seated Gala Dinner in the town hall of Vienna
Live Music and dance
End around 23:30
Dress Code: Black tie

CORLAS 2024 VIENNA

FAMILY DAY TOUR

Sunday, 25th August 2024

DÜRNSTEIN – WACHAU – MONASTERY MELK

TOUR:

Start	09:00	Hotel Palais Hansen, by bus to
Around	10:15	Dürnstein
11:15		Busdrive from Dürnstein to Spitz / Donau
11:45		Ship cruise on the Danube River along Wachau to City of Melk
Around	13:20	Arrival ship dock Melk
Around	13:30	Busstop Melk Monastery
Around	13:45	Lunch Monastery Restaurant Melk
14:45		Guided Tour through the monastery
16:30		Busdrive back to Vienna to Hotel Palais Hansen
Around	17:30	Arrival Hotel Palais Hansen

Costs:

Adults:	160 €
Children born 2012 and younger:	75 €

City Tour`s

Glorious Vienna – A Tour of Discovery

"The streets of Vienna are paved with culture, the streets of other cities with asphalt", writer and literary critic Karl Kraus once said about Vienna, and he is right. Vienna is one of the grandest capital cities in Europe, and one of the most compact, too. We discover the making of Vienna from Roman "Vindobona" to the capital of one of the largest empires in Europe. See the most famous landmarks and sights, amongst them the one-time Imperial Palace of the Habsburg family, the Viennese State Opera and all the nooks and crannies that make Vienna so Viennese.
Duration: around 2 ½ hours
Costs: free for registered members, guest, accompanying persons, children

Vienna's Grand "Boulevard of Splendor"- The Ringstrasse from State Opera to Votiv Church

In 1857, Emperor Franz Joseph decreed the demolition of Vienna's medieval fortifications. The idea of a 'Boulevard of Splendor' was born. The ‘Ring’, as the Viennese call it, became the imperial city’s greatest pride and building project, a work of art in itself, and unique in Europe. Today it is a designated UNESCO World Heritage Site. It is flanked by magnificent public buildings erected alongside the mansions of Vienna’s rising industrial and financial bourgeoisie, gardens and prancing monuments. We tell stories about the architects and their clients, anecdotes, and show historic photos.
Duration: about 2 hours
Costs: free for registered accompanying persons, children
For Members and Guests: 20 € (VAT included)

Art Nouveau: Gustav Klimt, Otto Wagner and the Secession

Vienna 1900 saw political stagnation and decadence, at the same time also a cultural and intellectual renaissance unparalleled in the modern world. Gustav Klimt, Otto Wagner and Josef Hoffmann, the most inspirational talents of the time, broke new grounds in the fields of architecture, painting and design. They seceded from Vienna's conservative, undistinguished art establishment and found their own art association. They called themselves "Secessionists" and named their newly-built exhibition hall with its laurel-leaf patterned dome Secession. "To each age its art, to art its freedom", was their motto. A rebirth of the arts and new concepts of design were what they were aiming at. Their legacy still lives on.

We start our tour with an introduction to Gustav Klimt's iconic Beethoven Frieze which was his contribution for an exhibition of the Secession honouring Beethoven. Originally located on the main floor, it was eventually moved to its present basement location where it is has been on permanent display since 1985. Its main theme is man's search for happiness and fulfilment which he finds in art, and of course, in Beethoven's music. We continue with three other iconic examples of Secessionist art, all by Otto Wagner, the father of Vienna's Modernist architecture: the Majolica House with its flowery tiled facade, stations he designed for the Vienna Metropolitan Line, and the Postal Savings Bank, a remarkable example of the rectilinear secessionist style.
Duration: about 2 hours
Costs: free for registered accompanying persons, children
For Members and Guests: 30 € (VAT included)

Jewish Vienna - In the Maelstrom of History

There have been Jewish communities in Vienna on and off since the 13th century, times of peace, religious freedom and prosperity but also times of growing anti-Semitism, persecution, expulsion and death. This illustrated tour offers an overview of the varying fates of the Viennese Jewry. Stops include the Simon Wiesenthal Institute for Holocaust Studies, the Community Centre of the IKG (Israelitische Kultusgemeinde, the Gestapo Memorial on Morzinplatz, and the Documentation Centre of the Austrian Resistance. The tour ends on Judenplatz where Rachel Whiteread's Holocaust Memorial next to the Jewish Museum commemorates the Austrian victims of the Shoah.
Duration: about 2 hours
Costs: free for registered accompanying persons, children instead of "Vienna`s Grand Boulevard"
For Members and Guests: 20 € (VAT included)

Schönbrunn Palace – Home of the Habsburg Dynasty

For 655 years Austria was ruled over by the House of Habsburg. Their domain reached from Hungary to Spain. Planned to rival the French palace of Versailles they commissioned Schönbrunn Palace to be built as their summer residence in their former hunting grounds outside Vienna.
Following the Spanish Court Ceremonial, more than 2.000 servants attended to their guests, maintained the huge baroque gardens, ran the kitchens and served as private valets of their majesties.
In some of the most beautiful State Rooms we explore public but also everyday life at the palace followed by a short stroll through the formal gardens.
Duration: Tuesday 13:00 – 16:00
Costs: 55 € (VAT included) for everybody
Minimum 20 participants

POST CONGRESS TOUR

Day 1: Thursday, 29th August 2024

VIENNA – HALLSTATT – FUSCHL AM SEE

Departure: 07:00 am Hotel Palais Hansen
Driving via motorway A1 to Hallstatt
Arrival in Hallstatt around 11:00 => guided tour through Hallstatt, lunch, guided tour through salt mine => Bus transfer to Fuschl am See Hotel Arabella Jagdhof Resort
Arrival around 18:30
Dinner

Day 2: Friday, 30th August2024

DAY IN SALZBURG

08:00	Departure from Hotel Arabella Jagdhof Resort Bus Transfer to Salzburg (around 30 minutes)
08:30	Arrival Salzburg Bus Terminal – Meeting Guides
09:00 / 09:15	Ride with the funicular to Fortress Hohen Salzburg => Viste of Fortress
10:15 / 10:30	Ride with Funicular down to the old city centre of Salzburg => Tour through the old city centre
11:00 / 11:15	Mozart´s birthplace
12:00	Lunch
13:45	Walk to Mirabell Garden
14:15 / 14:20	Bus Drive to Castel Hellbrunn => Tour through castel and garden

Day 3: Saturday, 31ST August 2024

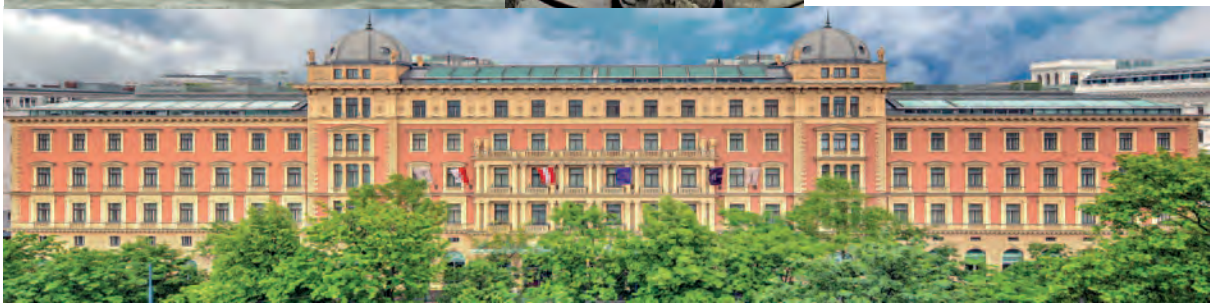
FUSCHL AM SEE – SWAROVSKI KRISTALLWELTEN - INNSBRUCK - KITZBÜHEL

Departure 07:30 from Hotel Arabella Jagdhof Resort

Bus transfer to Wattens / Tyrol and tour through Swarovski Kristallwelten.
Bus transfer to Innsbruck.
Visiting MED-EL Company and Lunch.

For those who will only participate 3 days => Transfer to Airport Innsbruck (INN)

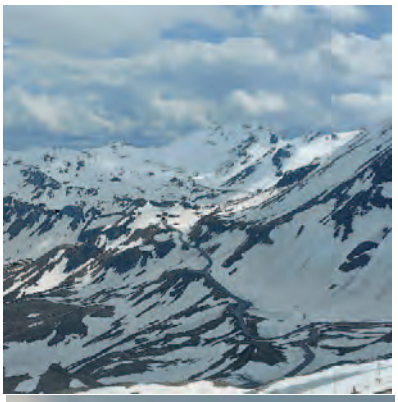
For those who will participate 4 days =>city tour through Innsbruck =>Bus transfer to Kitzbühel - Hotel Kitzhof Mountain Design Resort
Arrival around 18:00
Dinner

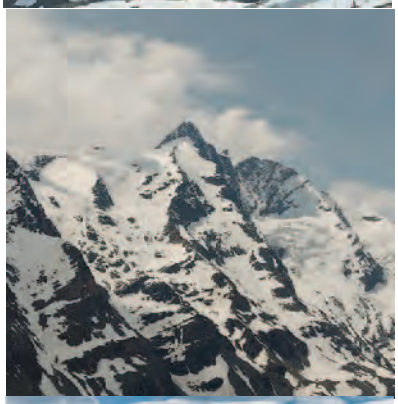


Day 4: Sunday, 01st September 2024

KITZBÜHEL – HEILIGENBLUT – GROßGLOCKNER HOCHALPENSTRAßE – VIENNA

For those, who would end in Kitzbühel, shuttle to Innsbruck or Munich airport possible (not included in tour fee)



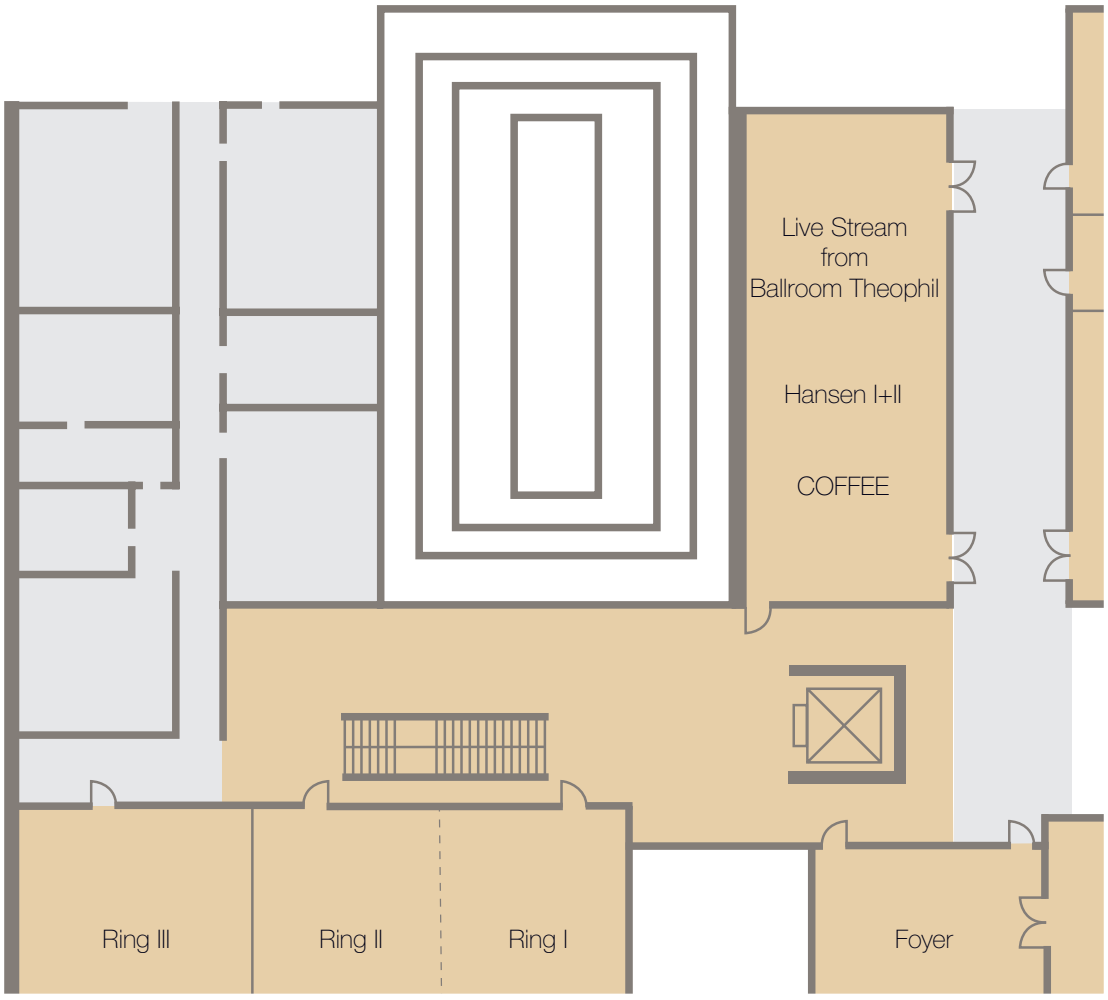


Departure 07:00 from Hotel Kitzhof Mountain Design Resort
Driving to Heiligenblut => Photo-stop at waterfall “Jungfernsprung”
Tour over Großglockner Hochalpenstraße with serveral photo stops
Lunch at the highest reachable point (2370 m) per bus – Panorama Restaurant Kaiser – Franz Josef Höhe
Tour over Großglockner Hochalpenstraße in direction to Ferleiten

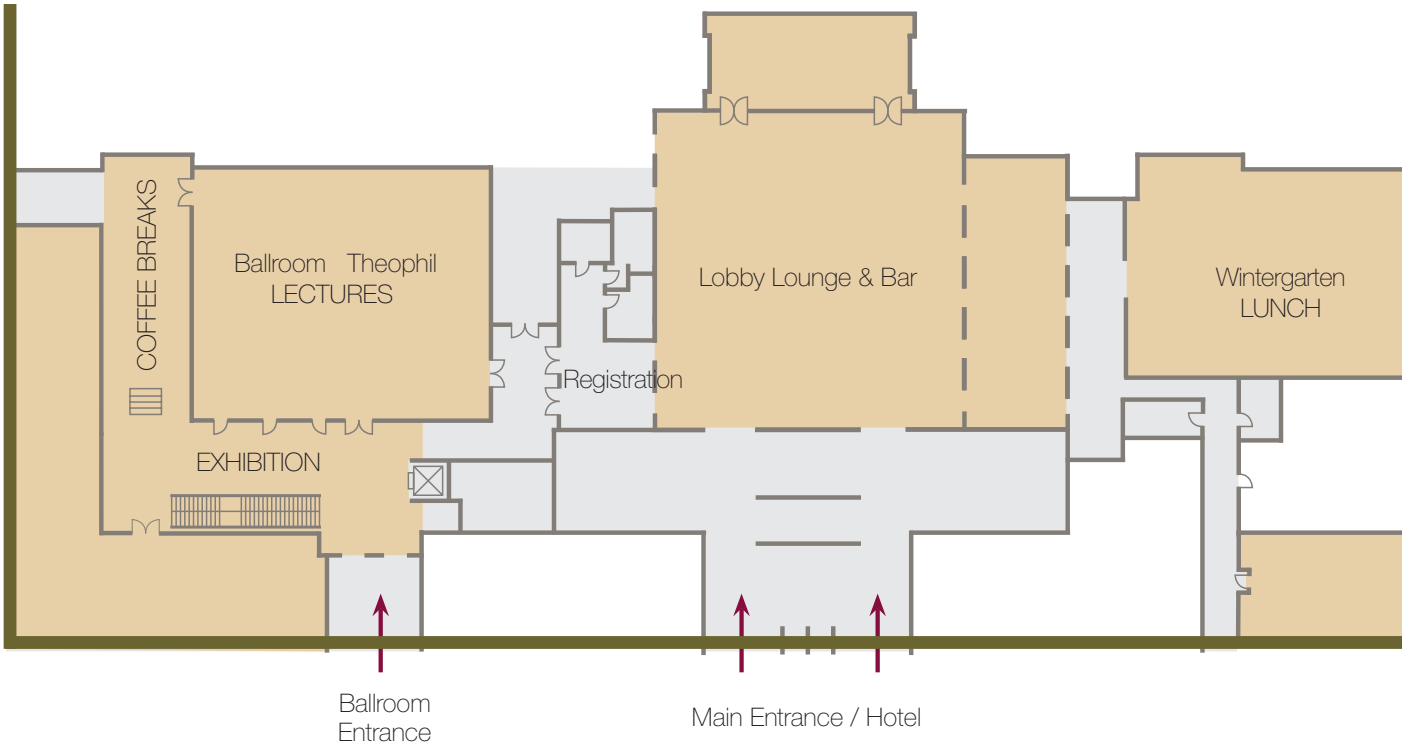
Driving to via Viennna
Arrival around 22:00

END OF TOUR

MEZZANINE / 1ST FLOOR



GROUNDFLOOR



CORLAS 2024 VIENNA

PROGRAM OVERVIEW

	Monday 26.08.2024	Tuesday 27.08.2024	Wednesday 28.08.2024
07:30-10:00	**Opening Ceremony** **Session 1** Head neck genetic	**Session 5** Vertigo **Session 6** Vertigo / Sleep	**Session 13** Fazialis Audiology **Session 14** Audiology and Tinnitus
10:00-10:30	**Coffee**	**Coffee**	**Coffee**
10:30-12:40	**Session 2** Cochlear Implant **Session 3** Cochlear Implant	**Session 7** Ear genetic **Session 8** Ear genetic	**Session 15** Ear genetic **Session 16** Ear genetic
12:40-13:40	**Lunch**	**Lunch**	**Lunch**

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	Monday 26.08.2024	Tuesday 27.08.2024	Wednesday 28.08.2024
13:40-15:30	**Session 4** Nose / FESS **General Assembly**	**Session 9** Head neck **Session 10** Head neck	**Session 17** Head neck **Session 18** Skull Base
15:45-16:00	**Bus**	**Coffee**	**Coffee**
16:00-18:00	**Concert in Golden Hall for the Musikverein Wien**	**Session 11** Cochlear Implant **Session 12** Cochlear Implant	**Session 19** Hearing Loss **Session 20** Otology
19:00-24:00	**Cultural Evening at the Heurigen Mayer am Pfarrplatz**	**Member´s and Accompanying Dinner in the Naturhistorical Museum and the Museum of fine arts**	**Gala Dinner in the historic festitive hall at Town Hall**

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CORLAS 2024 VIENNA

Monday, 26.08.2024 — **Saal Theophil**

Opening Ceremony — 08:00 – 08:50

Music - Festival Fanfare

Welcome	5 min	**CORLAS President** Wolf-Dieter Baumgartner (Vienna / Austria)
Welcome	5 min	**General Secretary Austrian ENT Society** Peter Franz (Vienna / Austria)
Welcome	5 min	**General Secretary of CORLAS** Antti Mäkitie (Helsinki / Finland)

Music - Ludwig van Beethoven

Introduction	3 min	**Jay Rubinstein** (Member, Seattle / USA)
Invited Lecture	20 min	**Promoting Innovation and Trust in Science without Borders** George Shambaugh (Georgetown / USA)

Music – *Antonio Vivaldi*

Monday, 26.08.2024 **Saal Theophil**

Session 1 – Head Neck Genetics 08:50 – 10:10

Chairs: Patrick Gullane (Member, Toronto / Canada)
Sandro Stöckli (Member, St.Gallen / Switzerland)

S1 L1 10 min **Collaborative Machine Learning-Guided Overall Survival Prediction of Oral Squamous Cell Carcinoma**
Antti Mäkitie (Member, Helsinki / Finland)

S1 L2 10 min **Integrated genomic and functional microRNA analysis identifies miR-30-5p as a tumor suppressor and novel therapeutic target in head and neck cancer**
Carter Van Waes (Member, Bethesda / USA)

S1 L3 10 min **Predictive role of PTHrP expression for effective anti-HER1 treatment in laryngeal squamous cell carcinomas**
Giovanni Almadori (Member, Rome / Italy)

S1 L4 10 min **Precision Oncology in Head and Neck Cancer Patients: Minimally Invasive, Maximally Functional**
Stephan Lang (Member, Essen / Germany)

S1 L5 10 min **Failure of drug delivery in human tumors caused by specific tumor and perivascular stromal elements**
Eben L Rosenthal (Member, Nashville / USA)

S1 L6 10 min **Monitoring disease status in patients with OPSCC by detection of cell-free HPV-DNA in liquid biopsies**
Jens Peter Klussmann (Member, Cologne / Germany)

S1 L7 10 min **Platelet-Derived Exosomes show distinct signaling properties**
Barbara Wollenberg (Member, Munich / Germany)

10 min ***Discussion***

20 min **Coffee Break**

Monday, 26.08.2024 **Saal Theophil**

Session 2 – Cochlear Implant Technology 10:30 – 11:40

Chairs: Kimitaka Kaga (Member, Tokyo / Japan)
George Wanna (Member, New York / USA)

S2 L1 10 min **Quantitative In-Vitro Assessment of a Novel Robot-Assisted System for Cochlear Implant Electrode Insertion**
Marco Caversaccio (Member, Berne / Switzerland)

S2 L2 10 min **Impact of Dexamethasone-Eluting Cochlear Implant Array on Longitudinal Electrode Impedance and Electrically Evoked Compound Action Potential Measures**
Bruce Gantz (Member, Iowa City / USA)

S2 L3 10 min **Unlocking the Cochlea with Synchrotron Phase-Contrast Imaging**
Sumit Agrawal (New Member, London / Canada)

S2 L4 10 min **A Seamless Approach to EAS and Conventional Cochlear Implantation**
Shin-ichi Usami (Member, Matsumoto / Japan)

S2 L5 10 min **A Totally Implantable Cochlear Implant shows potential benefits for adults with hearing loss**
Philippe Lefebvre (Member, Liege / Belgium)

S2 L6 10 min **OCT imaging for atraumatic Cochlear implant surgery**
Nicolas Verhaert (Guest, Leuven / Belgium)

10 min ***Discussion***

CORLAS 2024 VIENNA

Monday, 26.08.2024 **Saal Theophil**

Session 3 – Cochlear Implant Physiology *11*:40 – 12:40

Chairs: Andrej Kral (Member, Hanover / Germany)
Badr Eldin Mostafa (Member, Cairo / Egypt)

S3 L1 10 min **Intracochlear electrocochleography: insight into speech perception with a cochlear implant**
Stephen O'Leary (Member, Melbourne / Australia)

S3 L2 10 min **Assessment of cochlear nerve functionality in different vestibular schwannoma scenarios: insights gained for cochlear implantation**
Luis Lassaletta (New Member, Madrid / Spain)

S3 L3 10 min **Using focused thresholds to assess the electrode-neural interface in cochlear implants**
Andrew J. Oxenham (Member, Minneapolis / USA)

S3 L4 10 min **Perioperative impedance measurements provide novel insights into the health and function of the cochlea after implantation: a prospective cohort study**
Stephen O'Leary (Member, Melbourne / Australia)

S3 L5 10 min **Auditory Brainstem Implants: Are they Justified in Deaf Children with an Absent Cochlear-Nerve or Cochlea?**
Ronen Perez (Member, Jerusalem / Israel)

S3 L6 10 min **Cochlear Implantation for Single-Sided Deafness in Pediatric Patients: A Critical Assessment of Long-term Usage Rate**
Oliver F. Adunka (Member, Columbus / USA)

Monday, 26.08.2024 **Hotel Restaurant**

Lunch **12:40 – 13:40**

Lunch

CORLAS 2024 VIENNA

Monday, 26.08.2024 **Saal Theophil**

Session 4 – Rhinology 13:40 – 14:40

Chairs: Lars Olaf Cardell (Member, Stockholm / Sweden)
Antje Welge-Lüssen (Member, Basel / Switzerland)

S4 L1 10 min **Interferon signaling in the nasal epithelium distinguishes among lethal and common cold coronaviruses and mediates viral clearance**
Noam Cohen (Member, Philadelphia / USA)

S4 L2 10 min **Drug Repositioning for Nasal Polyp Therapy: Effects of HMG-CoA Reductase Inhibitors on Fibrinolytic System Activity**
Shigeharu Fujieda (Member, Fukuji / Japan)

S4 L3 10 min **Murine model of eosinophilic chronic rhinosinusitis using topical application of vitamin D3 analogue**
Kenji Kondo (Member, Tokyo / Japan)

S4 L4 10 min **Pediatric endonasal endoscopic skull base surgery: Long-term impact on sino-nasal outcome, olfaction, and facial development**
Cem Meco (Member, Ankara / Turkey)

S4 L5 10 min **The Role of Surgery in Orbitocranial Fungal Infection Treatment in the Era of Azole Antifungals**
Arkadi Yakirevitch (New Member, Tel Aviv / Israel)

S4 L6 10 min **Treatment of dilatory Eustachian tube dysfunction: From balloon dilation to absorbable stent and results of a randomized multicenter study**
Hong Ju Park (Member, Seoul / Korea)

CORLAS 2024 VIENNA

Monday, 26.08.2024 **Saal Theophil**

General Assembly 14:50 – 15:50

Chair: General Secretary Antti Mäkitie
Second Secretary Bradley Welling
President Wolf-Dieter Baumgartner

including

Preview 2025	3 min	**Stockholm**
Preview 2026	3 min	**Groningen**

16:00 on Time Bus Transfer to Musikverein

in front of Hotel Palais Hansen

Tuesday, 27.08.2024 **Saal Theophil**

Session 5 – Vestibular System 07:30 – 08:30

Chairs: Anil Lalwani (Member, New York / USA)
Stephen O´Leary (Member, Melbourne / Australia)

S5 L1 10 min **Transmastoid two-point plugging of superior semicircular dehiscence with preservation of vestibulo-ocular reflex**
Stefan K. Plontke (Member, Halle a. Saale / Germany)

S5 L2 10 min **Impact of Vibrations and Rapid Decelerations on SemontPLUS Maneuver Efficacy: An In Vitro Study**
Georgios Mantokoudis (New Member, Bern / Switzerland)

S5 L3 10 min **Digitally assisted sensorimotor brain stimulation for the therapy of Vertigo**
Hans Peter Zenner (Member, Tübingen / Germany)

S5 L4 10 min **Virtual Reality in Vestibular Assessment**
Maurizio Barbara (Member, Rome / Italy)

S5 L5 10 min **Effects of Meniere's treatments on vertigo frequency and endolymphatic space volume evaluated by using inner ear MRI**
Tadashi Kitahara (Member, Kashihara / Japan)

S5 L6 10 min **Vestivular Schwannoma Management in the 21st Century - emotional and other investments in decision making**
Shakeel Saeed (Member, London / Great Britain)

5 min ***Discussion***

Tuesday, 27.08.2024 **Saal Theophil**

Session 6 – Vertigo / OSAS / Olfactory 08:30 – 09:50

Chairs: Orlando Guntinas-Lichius (Member, Jena / Germany)
Sebastien Schmerber (Member, Grenoble / France)

S6 L1 10 min **Assessment and Time-Frequency Analysis for Gait Patterns Recognition in Unstable Older Patients with Vestibular Hypofunction**
Hamlet Suárez (Member, Montevideo / Uruguay)

S6 L2 10 min **Hearing and Vestibular Manifestations in Fabry Disease Patients: A Cross-Sectional Study in Taiwan**
Yen-Fu Cheng (Guest, Taipei / Taiwan)

S6 L3 10 min **Respiration-synchronized Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea: Historical background and Belgian results from the ADHERE registry**
Olivier M. Vanderveken (Guest, Antwerp / Belgium)

S6 L4 10 min **A Comparative Study of 11 Wearable, Nearable, and Airable Consumer SleepTrackers**
Jeong-Whun Kim (Member, Seoul / Korea)

S6 L5 10 min **Exploring temporal dynamics of subjective impairment and objective/subjective olfactory function in a cohort study of 524 patients**
Antje Welge-Lüssen (Member, Basel / Switzerland)

S6 L6 10 min **The role of MRI in post-traumatic olfactory dysfunction**
Basile N. Landis (New Member, Geneva / Switzerland)

S6 L7 10 min **Complex nasal reconstruction using forehead flap prelamination and 4D-CT angiography**
Nicole Rotter (Member, Mannheim / Germany)

10 min ***Discussion***

20 min **Coffee Break**

Tuesday, 27.08.2024 **Saal Theophil**

Session 7 – Hearing Genetics 10:10 – 11:30

Chairs: Hubert Löwenheim (Member, Tübingen / Germany)
Shin-Ichi Usami (Member, Matsumoto / Japan)

S7 L1 15 min **Precision Medicine and Gene Therapy for Hearing Loss and Vestibular Dysfunction**
Karen B. Avraham (Member, Tel Aviv / Israel)

S7 L2 10 min **The effects of epigenetic modifications on the efficacy of inner ear gene therapy**
Wade Chien (Guest, Bethesda / USA)

S7 L3 15 min **Developing new AAV vectors for inner ear disorders: rational design and directed evolution**
Hinrich Staecker (Member, Kansas City / USA)

S7 L4 15 min **Human otic progenitor cell models of congenital hearing loss reveal potential pathophysiologic mechanisms of Zika virus and cytomegalovirus infections**
Konstantina Stankovic (Member, Stanford / USA)

S7 L5 15 min **Gene therapy in a rabbit model for USH3A**
Yehoash Raphael (Member, Ann Arbor / USA)

S7 L6 10 min **Uncovering CHD7-SOX Gene Regulatory Networks to Advance the Diagnosis and Treatment of Genetic Hearing and Balance Disorders**
Donna Martin (Guest, Ann Arbor / USA)

Tuesday, 27.08.2024 **Saal Theophil**

Session 8 – Hearing Genetics II 11:30 – 12:40

Chairs: Karen Avraham (Member, Tel Aviv / Israel)
Michael McKenna (Member, Boston / USA)

S8 L1 10 min **Genetic Determinants of Hearing Loss and Cochlear Implant Outcomes in a Comprehensive German Cohort Study**
Anke Tropitzsch (Guest, Tübingen / Germany)

S8 L2 10 min **Lgr5+ endogenous progenitor cells in the human and mouse adult (deafened) cochlea**
Robert J. Stokroos (Member, Utrecht / T. Netherlands)

S8 L3 10 min **Preclinical development of vesicle-enriched secretome fractions for the prevention of cochlear implantation trauma**
Athanasia Warnecke (Member, Hanover / Germany)

S8 L4 10 min **Efficacy of Small-Molecule Kv7.4 Agonist ACOU-085 in Protecting Against Cisplatin-Induced and Age-Related Hearing Loss**
Hubert Löwenheim (Member, Tübingen / Germany)

S8 L5 10 min **Regulatory network of mTORC2 in an auditory hair cells line**
Daniel Bodmer (Member, Basel / Switzerland)

20 min ***Discussion***

Tuesday, 27.08.2024 **Hotel Restaurant**

Lunch **12:40 – 13:40**

Lunch

Tuesday, 27.08.2024 **Saal Theophil**

Session 9 – Head Neck I 13:40 – 14:50

Chairs: Carol Bradford (Member, Columbus / USA)
Robert L Ferris (Member, Pittsburgh / USA)

S9 L1 10 min **Tumor tissue hnRNP M as a potential biomarker of disease-specific mortality in patients with early-stage cutaneous head and neck melanoma: A proteomics-based study**
Andro Košec (Member, Zagreb / Croatia)

S9 L2 10 min **Application of artificial intelligence in endoscopic diagnosis of glottic lesions**
Taku Yamashita (Member, Tokyo / Japan)

S9 L3 10 min **Intraoperative nerve-specific fluorescence imaging: first in-human results**
Quyen T. Nguyen (Member, San Diego / USA)

S9 L4 10 min **Ultrasound guided procedures in the Head and Neck: A clinician centered model**
Francesco Bussu (Member, Sassari / USA)

S9 L5 10 min **3D-image-guided navigation with touchless gesture user interface during minimally invasive head and neck surgery: do we have "biomechanics" of the new era in our personalized contactless hand-gesture non-invasive surgeon-computer interaction?**
Ivica Klapan (Member, Osijek / Croatia)

S9 L6 10 min **Usefulness of ultra high-resolution computed tomography for preoperative staging of the tongue cancer**
Ichiro Tateya (Member, Toyoake / Japan)

10 min ***Discussion***

Tuesday, 27.08.2024 **Saal Theophil**

Session 10 – Head Neck II 14:50 – 16:00

Chairs: Elisabetta Zanoletti (Member, Padova / Italy)
Koichi Omori (Member, Kyoto / Japan)

S10 L1 10 min **Extracapsular dissection in benign parotid gland tumors: single institution experience**
Heinrich Iro (Member, Erlangen / Germany)

S10 L2 10 min **Modern Thyroid Surgery and Parathyroid gland Vasculature preservation during total Thyroidectomy**
Hani Z. Marzouki (New Member, Jeddah / Saudi Arabia)

S10 L3 10 min **Endoscopic laryngopharyngeal surgery for early stage hypopharyngeal cancers**
Yo Kishimoto (New Member, Kyoto / Japan)

S10 L4 10 min **Reconstruction of a tracheal defect using a 3D printed leaf-stacked scaffold implanted with mesenchymal stem cell spheroids**
Seong Keun Kwon (Member, Seoul / Korea)

S10 L5 10 min **Carotid Body Tumors: Association between SDHB Immunohistochemistry Results and Genetic Testing**
Hiroyuki Ozawa (Member, Tokyo / Japan)

S10 L6 10 min **Long-term survival in pediatric tracheostomy with different socioeconomic status: A population-based study**
Wei-Chung Hsu (Member, Taipei / Taiwan)

10 min ***Discussion***

10 min **Coffee Break**

Tuesday, 27.08.2024 **Saal Theophil**

Session 11 – Cochlear Implant I 16:10 – 17:10

Chairs: Marco Caversaccio (Member, Berne / Switzerland)
Bruce Gantz (Member, Iowa City / USA)

S11 L1 10 min **The Development of a Newly Invented Inner Ear Implant Device (HIBIKI): Results of animal experiment**
Juichi Ito (Member, Kyoto / Japan)

S11 L2 10 min **Investigation of Local Dexamethasone Delivery Techniques to the Inner Ear in a Large Animal Model**
Christoph Arnoldner (Member, Vienna / Austria)

S11 L3 10 min **Does Cochlear Implant Electrode Array Design Affect Audiologic Outcomes? A Systematic Review and Meta-Analysis**
Robert F. Labadie (Member, Charleston / USA)

S11 L4 10 min **FLEX 34 – cochlear implant electrode: first experience and results**
Wolf-Dieter Baumgartner (Member, Vienna / Austria)

S11 L5 10 min **X-ray Guided Anatomy-Based Fitting**
Abdulrahman Hagr (Member, Riyadh / Saudi Arabia)

S11 L6 10 min **The application of the exoscope in Otorhinolaryngology: Case Cochlear Implantation**
Aarno Dietz (New Member, Kuopio / Finland)

Tuesday, 27.08.2024 **Saal Theophil**

Session 12 – Cochlear Implant II **17:10 – 18:10**

Chairs: Tatsuya Yamasoba (Member, Tokyo / Japan)
Marlan Hansen (Member, Iowa City / USA)

S12 L1 10 min **Identification of Potential Candidates for CI in a large data base of Hearing Aids users**
Bernard Fraysse (Member, Toulouse / France)

S12 L2 10 min **Long-term outcome of cochlear implantation in children with cochlear nerve deficiency**
Bee-See Goh (Member, Kuala Lumpur / Malaysia)

S12 L3 10 min **Cochlear implantation in patients with mumps-related hearing loss**
Piotr Skarzynski (Member, Warsaw / Poland)

S12 L4 10 min **Cochlear implantation in syndromic patients: difficulties and lessons learnt**
Badr Eldin Mostafa (Member, Cairo / Egypt)

S12 L5 5 min **Early auditory development of cochlear implanted children with sensorineural hearing loss following congenital CMV infection**
Henryk Skarzynski (Member, Warsaw / Poland)

S12 L6 10 min **Outcomes of cochlear implantation compared to auditory brainstem implantation in cochlear nerve deficiency**
Tamer Mesallam (Member, Riyadh / Saudi Arabia)

S12 L7 10 min **International consensus on intraoperative testing for cochlear implantation & the recommended minimum intraoperative testing battery**
Farid Alzhrani (New Member, Riyadh / Saudi Arabia)

Wednesday, 28.08.2024 **Saal Theophil**

Session 13 – Facialis, Tinnitus, Audiology **07:30 – 08:40**

Chairs: Paul van de Heyning (Member, Antwerp / Belgium)
Ashley Wackym (Member, New Brunswick / USA)

S13 L1 10 min **Facial functional electrical stimulation to prevent denervated muscle atrophy in patients with facial paralysis - the road to clinical routine**
Orlando Guntinas-Lichius (Member, Jena / Germany)

S13 L2 10 min **Tinnitus in patients with orofacial complaints**
Tobias Kleinjung (Member, Zurich / Switzerland)

S13 L3 10 min **Tinnitus and GABA receptors in the auditory cortex: a PET study**
Pim van Dijk (Member, Groningen / The Netherlands)

S13 L4 10 min **Development and Validation of an Outcomes Measure for the Hearing-impaired Children and Parents**
Pa-Chun Wang (Member, Taipei / Taiwan)

S13 L5 10 min **Premature test termination in a German matrix speech test in noise**
Martin Kompis (Member, Bern / Switzerland)

S13 L6 10 min **Influence of simulated adverse events of the Floating mass transducer in a mechanical middle ear model**
Christof Stieger (Member, Basel / Switzerland)

S13 L7 10 min **Better understanding of surgical video of mastoidectomy by Video inpainting and Stabilization using artificial intelligence**
Jong Woo Chung (Member, Seoul / Korea)

Wednesday, 28.08.2024 **Saal Theophil**

Session 14 – Audiology 08:40 – 09:55

Chairs: Allen Ryan (Member, La Jolla / USA)
Maurizio Barbara (Member, Rome / Italy)

S14 L1 15 min **Cognitive impact of hearing loss in absence of language**
Andrej Kral (Member, Hanover / Germany)

S14 L2 10 min **How the gut microbiome can influence hearing? New insight on a gut-cochlear axis**
Anna Rita Fetoni (Member, Naples / Italy)

S14 L3 10 min **Desynchronization of auditory development from sensory and motor systems in the first years of life of a deaf baby: Cochlear implant at nine months may not be early enough**
Liat Kishon-Rabin (Guest, Tel Aviv / Israel)

S14 L4 10 min **Machine learning-based longitudinal prediction for GJB2-related sensorineural hearing loss**
Chen-Chi Wu (Member, Taipei / Taiwan)

S14 L5 10 min **Interpretation of psychophysical tests from computational models**
Jeroen Briaire (Member, Leiden / The Netherlands)

S14 L6 10 min **Hearing Health Strategy: the Hearing Health Forum EU Manifesto**
Paul Van de Heyning (Member, Antwerp / Belgium)

10 min ***Discussion***

20 min **Coffee Break**

Wednesday, 28.08.2024 **Saal Theophil**

Session 15 – Hearing Genetics III 10:15 – 11:25

Chairs: Konstantina Stankovic (Member, Stanford / USA)
Yehoash Raphael (Member, Ann Arbor / USA)

S15 L1 15 min **Clinical development of AK-OTOF gene therapy for *OTOF*-mediated hearing loss**
Michael J. McKenna (Member, Boston / USA)

S15 L2 15 min **The Phoenix platform as novel tool to unveil regenerative pathways in presenescent auditory neuroprogenitors**
Pascal Senn (Member, Geneva / Switzerland)

S15 L3 10 min **Exploring Hereditary Deafness: Unveiling Insights with Human-Induced Pluripotent Stem Cells**
Brigitte Malgrange (Member, Liege / Belgium)

S15 L4 10 min **Preservation of Residual Hearing and Enhancing Cochlear Implant Outcomes with Drug Y: A Novel Approach to Otoprotection and Neurite Outgrowth**
Adrien A. Eshraghi (Member, Miami / USA)

S15 L5 10 min **The Varieties of Otoferlin-related Phenotype**
Rosamaria Santarelli (Member, Padova / Italy)

10 min ***Discussion***

Wednesday, 28.08.2024 **Saal Theophil**

Session 16 – Hearing Genetics IV 11:25 – 12:30

Chairs: Pascal Senn (Member, Geneva / Switzerland)
Hinrich Staecker (Member, Kansas City / USA)

S16 L1 10 min **Combinatorial Protection of Cochlear Hair Cells: Not Too Little, But Not Too Much**
Allen F Ryan (Member, San Diego / USA)

S16 L2 10 min **Disease-modifying therapy for autosomal dominant hereditary hearing loss in DFNA9**
Vincent Van Rompaey (Guest, Antwerp / Belgium)

S16 L3 10 min **An AAV-based antioxidative gene therapy to prevent and treat noise-induced hearing loss**
Todd M Mowery (Guest, New Brunswick / USA)

S16 L4 10 min **Elucidation of Inner Ear Development Mechanisms from Single-cell Genomic Data**
Norio Yamamoto (Member, Kobe / Japan)

S16 L5 10 min **Auditory neuropathy and related phenotypes associated with m.7471dup variant in MT-TS1**
Tatsuo Matsunaga (Member, Tokyo / Japan)

10 min ***Discussion***

Wednesday, 28.08.2024 **Hotel Restaurant**

Lunch **12:30 – 13:30**

Lunch

Wednesday, 28.08.2024 **Saal Theophil**

Session 17 – Head Neck Oncology I 13:30 – 14:40

Chairs: Ichiro Tateya (Member, Toyoake / Japan)
Jens P Klussmann (Member, Cologne/ Germany)

S17 L1 15 min **Management of the Unknown Head and Neck Primary in the Era of TORS**
C. René Leemans (Member, Amsterdam / Netherlands)

S17 L2 10 min **A quantitative approach reveals a different look at distant metastasis**
Robert J Baatenburg de Jong (Member, Rotterdam / The Netherlands)

S17 L3 10 min **Towards organ preservation via immunotherapy in patients normally undergoing extensive curative surgery and radiotherapy**
Lotje Zuur (New Member, Amsterdam / T. Netherlands)

S17 L4 10 min **Discrete prognostic implication of sarcopenia according to nutritional status in surgically treated patients with hypopharyngeal cancer**
Yoon Se Lee (Member, Seoul / Korea)

S17 L5 10 min **Prognostic significance of metabolic tumor volume in patients with recurrent and/or metastatic head and neck squamous cell carcinoma**
Yukinori Takenaka (New Member, Osaka / Japan)

S17 L6 10 min **Transoral videolaryngoscopic surgery (TOVS) for elderly patients with laryngopharyngeal cancer**
Kosuke Uno (Guest, Tokyo / Japan)

5 min ***Discussion***

Wednesday, 28.08.2024 **Saal Theophil**

Session 18 – Otology / Varia 14:40 – 15:50

Chairs: C. René Leemans (Member, Amsterdam / The Netherlands)
Claes Möller (Member, Örebro / Sweden)

S18 L1 10 min **Streptococcus angionosus group, much more than commensals**
Ann Hermansson (Member, Lund / Sweden)

S18 L2 10 min **Head and neck cancer treatment based on medical-dental collaboration**
Mizuo Ando (Member, Okayama / Japan)

S18 L3 10 min **Possible Mechanism of Carcinogenesis of Temporal Bone Squamous Cell Carcinoma**
Takashi Nakagawa (Member, Fukuoka / Japan)

S18 L4 10 min **Whiteish color change around the FAF in otosclerosis**
Tatsuya Yamasoba (Member, Tokyo / Japan)

S18 L5 10 min **Appropriate Ossicle Palpation during Otologic Surgery: Variations in Judgments and How Surgeons Exert a Large Force on the Ossicles**
Sho Kanzaki (Member, Tokyo / Japan)

S18 L6 10 min **Assessment and management of postoperative pain in pediatric otolaryngology**
Tomasz Zatonski (Member, Wrocław / Poland)

S18 L7 10 min **Direct Microneedle Intracochlear Injection of Gadodiamide through the Round Window Membrane Enables Rapid Intracochlear Imaging on MRI**
Anil K. Lalwani (Member, New York / USA)

10 min **Coffee Break**

Wednesday, 28.08.2024 **Saal Theophil**

Session 19 – Hearing Loss 16:00 – 17:00

Chairs: Stefan Plontke (Member, Halle/Saale / Germany)
Philippe Levebvre (Member, Liege / Belgium)

S19 L1 10 min **Transmastoid superior semicircular canal dehiscence plugging: VHIT findings**
Romain Kania (Member, Paris / France)

S19 L2 10 min **What is the most important factor to preserve hearing in lateral semicircular canal fistula surgeries, fistula size or bony structure?**
Jeonghun Jang (Guest, Suwon / Korea)

S19 L3 10 min **How can we distinguish angiopathic sudden sensorineural hearing loss from the others?**
Koichiro Wasano (Guest, Tokyo / Japan)

S19 L4 10 min **Hyperacusis after noise-induced hearing loss: mechanisms, biomarkers, and proof-of-concept treatment**
Daniel B. Polley (New Member, Boston / USA)

S19 L5 10 min **Auditory Agnosia Caused by Bilateral Auditory Cortex Lesions due to Herpes Encephalitis of An Infant but Cortical Deafness at Period of Teenager Presenting Profound Hearing Loss with Normal ABR and DPOAE-37 years follow up**
Kimitaka Kaga (Member, Tokyo / Japan)

S19 L6 10 min **Clinical Impact of Hyperbaric Oxygen Therapy Combined with Steroid Treatment for Sudden Sensorineural Hearing Loss: a case-control study**
Shinichi Iwasaki (Member, Nagoya / Japan)

Wednesday, 28.08.2024 **Saal Theophil**

Session 20 – Otology 17:00 – 18:10

Chairs: Shakeel Saeed (Member, London / UK)
Christophe Vincent (Member, Lille / France)

S20 L1 10 min **Usher Syndrome - Past, Present and Future**
Claes Möller (Member, Örebro / Sweden)

S20 L2 10 min **Navigation in temporal bone and lateral skull base surgery**
Marc Bassim (New Member, Beirut / Lebanon)

S20 L3 10 min **A multi-omics evaluation of the microbiome in oral cavity squamous cell carcinoma**
Jason Y K Chan (New Member, Hong Kong / China)

S20 L4 10 min **Repair of spontaneous cerebrospinal otorrhea using middle fossa approach**
Kadir Serkan Orhan (Member, Istanbul / Turkey)

S20 L5 10 min **Prognostic Factors in Myringoplasty**
Nicola Quaranta (Member, Bari / Italy)

S20 L6 10 min **Access to the provision of hearing health in patients with presbycusis: A new model of care for public health insurance in Chile**
Mariela C. Torrente (Member, Santiago / Chile)

S20 L7 10 min **Exploring Arctic Acoustics: Otology's Frontier in Greenland**
Ramon Gordon Jensen (New Member, Copenhagen / Denmark)

Closing Ceremony
Peter Franz
CORLAS Vice President

S1 L1 - Collaborative Machine Learning-Guided Overall Survival Prediction of Oral Squamous Cell Carcinoma

Antti Mäkitie, Rasheed Omobolaji Alabi, Alhadi Almangush, Mohammed Elmusrati, Ilmo Leivo
Department of Otorhinolaryngology – Head and Neck Surgery, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

Background: The incidence rate of Oral Squamous Cell Carcinoma (OSCC) shows a marked increase in the Western world. The occurrence of recurrences, and the high mortality ratio continue to be a challenge. Therefore, a concise effort is needed to predict OSCC tumor behavior and overall survival (OS). However, there still is a lack of specific prognostic indicators.

Objectives: This study aimed at examining the potential of a collaborative machine learning (cML) -based approach in estimating the OS of OSCC patients. In addition, the prognostic significance of the clinicopathological parameters used to develop the model was examined.

Methodology: The clinicopathological information of 7231 OSCC patients were extracted from the Surveillance, Epidemiology, and End Results (SEER) database, United States. A total of five machine learning (ML) models – extreme gradient boosting (XGBoost), logistic regression (LR), gradient boosting (GB), linear Support Vector Machine (Linear SVM), and voting ensemble (VE) were combined to form a collaborative cluster of ML (CCML) models. The performance of the CCML was compared with the voting ensemble algorithm.

Results: The performance accuracy of XGBoost, LR, GB, Linear SVM, VE, and CCML models was 81.7%, 71.3%, 79.4%, 76.1%, and 90.1%, respectively. The results showed that the CCML outperformed individual ML algorithms and the voting ensemble ML paradigm. The age of the patient, T class of the tumor, radiotherapy, and surgical resection were among the significant prognostic factors.

Discussion and Conclusions: The cML approach combines the individual properties and abilities of each ML algorithm in estimating the OS of OSCC patients. Considering the significant burden associated with OSCC and the corresponding treatment sequelae, effective and improved prediction of OS of OSCC may help in the management planning of the disease. The cML approach may aid in determining individualized treatment for OSCC patients.

***S1 L2* - Integrated genomic and functional microRNA analysis identifies miR-30-5p as a tumor suppressor and novel therapeutic target in head and neck cancer**

Anthony D. Saleh, Charles Marusak, Clint T. Allen, and Carter Van Waes
National Institute on Deafness and Other Communication Disorders, National Cancer Institute, National Institutes of Health, Bethesda, Maryland and miRecule, Inc., Gaithersburg, Maryland, USA

Purpose and Experimental Design: microRNA (miRNA, miR) plays a key role in regulating the extent and duration of expression of mRNAs and encoded proteins critical in health and disease. Deregulated miRNA can unleash overexpression of multiple mRNAs and encoded proteins that promote cancer pathogenesis, and resistance to therapies devised against individual targets. To identify deregulated inhibitory miRNAs and generate novel mimics for miR replacement for head and neck squamous cell carcinomas (HNSCC), we integrated miRNA and mRNA expression, copy number variation, and DNA methylation results from The Cancer Genome Atlas (TCGA), with a functional genome-wide miR screen.

Results: We reveal that the miR-30 family, which includes 5 members that share homologous seed sequences, are repressed in ~60% of HNSCC. Significantly decreased miR-30 family expression was related to DNA gene deletion (~30%) and promoter hypermethylation (~20%), and clinically with decreased disease-specific survival in TCGA and an independent validation dataset. Strikingly, decreased miR-30 distinguished oropharyngeal carcinomas (OPC) with poor prognosis in TCGA ($p=0.002$) and validation ($p=0.007$) datasets, identifying a novel candidate biomarker and target for this HNSCC subset. miR-30 expression was inversely related with overexpression of a network of important predicted target mRNAs deregulated in HNSCC. This network includes key molecules implicated in cell proliferation (EGFR, IGF1R, IRS1, E2F7), differentiation (WNT7B, FZD2), adhesion, invasion, and metastasis (ITGA6, SERPINE1, MET). Re-expression of the most differentially repressed family member, miR-30a-5p, suppressed this mRNA program, selected signaling proteins and pathways, and inhibited cell proliferation, migration, and invasion in vitro. miRecule's NAVIgGator platform has enabled development of a novel chemically modified mimic of miR-30-5p, that is delivered to HNSCC tumors systemically via conjugation to the anti-EGFR antibody cetuximab. This Antibody RNA Conjugate, MC-30, overcomes the known mechanisms of resistance of cetuximab, and has the potential to deliver effective long-term maintenance of disease suppression in HNSCC.

Conclusions: We identify the miR-30 family as an important regulator of signal networks and tumor suppressor in a subset of HNSCC and OPC patients, that may benefit from antibody targeted miR conjugate replacement therapy.

S1 L3 - Predictive role of PTHrP expression for effective anti-HER1 treatment in laryngeal squamous cell carcinomas

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In laryngeal tumors, EGFR expression has been associated with a poor prognosis. Furthermore, therapeutic resistance to anti-HER1 therapy may arise from alternative pathways overcoming the reduced HER1 signaling and/or modulating the HER1-dependent signaling. It has been observed that HER1 signaling regulates PTHrP gene expression in a variety of normal and cancer cell types, contributing to the malignancy of tumor cells downstream of HER1 signaling.In our cohort of laryngeal squamous cell carcinomas (LASCC) patients, treated with bio- radiotherapy with cetuximab, expression of nuclear PTHrP seems to be a prognostic/predictive marker of relapse and poor survival. Furthermore, we found that HER1 and PTHrP were coexpressed, particularly in poorly differentiated laryngeal tumors. In particular, 55% (28/51) of LASCCs co-expressed HER1 and PTHrP while 16% (8/51) expressed HER1 in the absence of PTHrP. Using survival analysis, we observed that patients with the HER1+/PTHrP+ LSCC phenotype had a significantly lower loco-regional metastasesfree survival (Log-Rank test: p= 0.012) and a higher relative risk (HR: 6.93; 95% CI: 1.44 - 68.3) compared to patients with HER+/PTHrP- LSCC. Since predictive biomarkers for effective antiHER1 treatment in HNSCC are important for personalized therapy and considering that PTHrP can contribute to an aggressive behavior of tumor cells downstream to HER1, it seems important to evaluate in LSCC the expression of PTHrP in predicting resistance to cetuximab-combined treatment.

S1 L4 - Precision Oncology in Head and Neck Cancer Patients: Minimally Invasive, Maximally Functional

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Precision oncology comprises several important areas, all of which are fully implemented in our innovative operating theater:

1.Virtual Reality:
Precise surgical planning is essential, especially for complex tumors of the skull base. By converting CT and MRI data sets into three-dimensional structures and then viewing them using virtual reality (VR) glasses, a three-dimensional representation of the corresponding structures is possible thus helping to select the best surgical approach.

2. Artificial Intelligence (AI):
For the use of VR-based surgical planning, but also the preoperative visualization of complex lesions and anatomy we use corresponding planning software, which automatically generates a two- or three-dimensional model of the respective lesion using a special AI technology based on a patented synthetic tissue model.

3. 4K 3D Visualization:
A 4K 3D camera enables precise surgery by displaying even the smallest tissue structures. Compared to Full HD, the advantage here is the four times higher resolution and the working distance of just 1.5 meters to the 55” monitor.

4. Robotics:
A Robot-assisted visualization device based on a view-changing full digital 3D microscope together with a head-Mounted Display (HMD) and robotic arm enables us to perform Augmented Reality operations with online feedback about nerval functions thus preserving function and quality of life as well.

Conclusion:
Digital innovations are opening up new possibilities in medicine, and particularly in the operating theater, which were previously only possible in future scenarios: The individual components of the operating theatre environment, from preparation and planning to the execution of surgical therapy, are being networked, automated and digitized. Thus, enabling us to perform minimally invasive surgery with maximum care.

***S1 L5* - Failure of drug delivery in human tumors caused by specific tumor and perivascular stromal elements**

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Improving clinical outcomes with targeted therapeutics requires a comprehensive understanding of drug-target-microenvironment interactions. Using a fluorescently labeled therapeutic antibody, we were able to assess barriers to delivery in a human tumor. We conducted a first-in-human clinical study to directly measure drug-target engagement in single cells and drug penetration depth in head and neck cancer patients. Since the systemically administered labeled therapeutic antibody could be located at high resolution within these tumors, we identified significant heterogeneity of drug delivery – differences we exploited to investigate delivery of the drug within areas of high and low drug concentration. We discovered that the spatial arrangement of specific ECM matrices (collagen I-periostin and periostin-collagen I-fibronectin) that are produ, and two cellular neighborhoods enriched in FAP+ and FAP+/CD73+ cancer-associated fibroblasts (CAFs) act as barriers to the delivery of therapeutic antibodies. We found FAP+CAFs produce an extracellular matrix (ECM) network of collagenI-periostin that limits the penetration of anti-EGFR antibodies to reach the tumor cell. Also contributing to heterogeneity of drug delivery is the presence of periostin-collagenI-fibronectin matrix produced by FAP+/CD73+ CAFs surrounding and constricting the microvasculature in areas of low drug delivery. We propose this as a new framework for interrogating drug pharmacology in the context of tumor biology, opening new avenues for dosing optimization, biomarker identification, and drug development.

S1 L6 - Monitoring disease status in patients with OPSCC by detection of cell-free HPV-DNA in liquid biopsies

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Background: Human Papilloma Virus (HPV)-associated oropharyngeal squamous cell cancer (OPSCC) represents an OPSCC subgroup with an overall good prognosis with a rising incidence in Western countries. Novel technologies allow the detection of minimal amounts of circulating cell-free HPV DNA (cfHPV-DNA). The aim of this study was to evaluate cfHPV-DNA assessed by droplet digital PCR (ddPCR) and quantitative PCR (qPCR) as a biomarker for molecular therapy monitoring in HPV-driven OPSCC.
Methods: We examined 48 patients with HPV-related OPSCC (HPV16DNA+/p16+) and 21 controls (healthy donors and HPV-negative OPSCC patients) to investigate cfHPV16-DNA status prior to and during therapy as well as throughout follow-up. qPCR and ddPCR were applied to quantify the concentration of cfHPV16-DNA in plasma, using the viral gene E6 as a target. Overall, 406 blood sample were tested. Beside baseline, blood was taken 2.6 – 157.8 month after diagnosis (mean 19.2 month). Further virus load was measured in the corresponding primary tumors and compared to cfHPV-DNA levels.
Results: No cfHPV16-DNA or <10 copies per ml plasma were detected in healthy donors or HPV-negative OPSCC patients. Plasma samples from patients with HPV-positive OPSCC collected prior to treatment. At the cut-off of 10 copies/ml plasma, ddPCR showed 82% sensitivity, 80% specificity, 70% NPV, and 90% PPV, whereas qPCR showed 73% sensitivity, 80% specificity, 63% NPV, 91% PPV. cfHPV16-DNA copies (ddPCR) at first diagnosis correlate significantly with tumor stage, tumor volume (CT and MRT) and PET-CT parameters. Further a significant correlation of tumor viral load (L1) in tumor tissue with cfHPV16-DNA copies was found ($P<0.01$). Patients without clinical evidence of recurrence had significantly lower cfHPV16-DNA concentrations after therapy, whereas increase of copy number was correlated to recurrent disease. Detection of cfHPV16-DNA after curative treatment was correlated to worse prognosis.
Discussion and Conclusions: Results demonstrate that ddPCR is a more sensitive method compared to qPCR for detection of cfHPV16-DNA in plasma of patients with HPV16-positive OPSCC. cfHPV16-DNA correlated with tumor burden and tumor relapse and therefore presents a promising diagnostic tool. It has to be taken into account, that the cfHPV16-DNA levels correlate to HPV copy numbers in the tumor cells. Therefore, a standardization of the diagnostic procedure is necessary before introducing liquid biopsy into the clinical routine. In the future, this might allow surveillance and detection of minimal residual disease in HPV-positive OPSCC.

S1 L7 - Platelet-Derived Exosomes show distinct signaling properties

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Background:
Exosomes are small extracellular vesicles (30-150 nm) that play a crucial role in intercellular communication by transporting proteins, lipids, and genetic material between cells. Platelet-derived exosomes (PDEs) are a subset of exosomes released from activated platelets, which are abundant in the bloodstream and involved in hemostasis and thrombosis. The study of PDEs has gained significant attention due to their potential involvement in various physiological and pathological processes.
Objective:
This abstract aims to provide an overview of the current understanding of platelet-derived exosomes, their biogenesis, molecular composition, and potential roles in health and disease.
Methods:
A comprehensive review of recent literature was conducted to summarize the biogenesis of PDEs, their molecular cargo, and the techniques used for their isolation and characterization. Additionally, the functional roles of PDEs in different biological contexts were examined, focusing on their involvement in coagulation, immune response, and disease mechanisms.
Results:
Biogenesis and Isolation: PDEs are formed through the endosomal pathway and released upon platelet activation. Techniques such as ultracentrifugation, size-exclusion chromatography, and immunoaffinity capture are commonly employed for their isolation.
Molecular Composition: PDEs contain a variety of bioactive molecules, including proteins (e.g., integrins, CD40L), lipids (e.g., phosphatidylserine), and nucleic acids (e.g., miRNAs, mRNAs). The molecular composition reflects the cellular origin and the activation state of the platelets.
Functional Roles:
Coagulation: PDEs contribute to hemostasis by providing a surface for coagulation factor assembly and by transferring pro-coagulant molecules.
Immune Response: PDEs modulate the immune system by influencing the function of immune cells, such as dendritic cells and macrophages, and by carrying immune-related molecules.
Disease Mechanisms: PDEs are implicated in various diseases, including cardiovascular diseases, cancer, and inflammatory conditions. They can promote angiogenesis, tumor growth, and metastasis, as well as influence the inflammatory response.

Conclusion:
Platelet-derived exosomes represent a significant component of the extracellular vesicle population with diverse biological functions. Understanding the roles of PDEs in health and disease could open new avenues for diagnostic and therapeutic strategies. Future research should focus on elucidating the mechanisms of PDE-mediated communication and exploring their potential as biomarkers and therapeutic targets in various clinical settings.

S2 L1 - Quantitative In-Vitro Assessment of a Novel Robot-Assisted System for Cochlear Implant Electrode Insertion

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As an increasing number of cochlear implant candidates exhibit residual inner ear function, hearing preservation strategies during implant insertion are gaining importance. Traditional manual implantation can induce traumatic force and pressure peaks due to limitations in achieving slow, consistent insertion speeds. In this study, in a validated in-vitro model, we comprehensively evaluate a novel surgical tool that addresses these challenges through motorized movement. Using lateral wall electrodes, we examined two subgroups of insertions: 30 insertions were performed manually by experienced surgeons, and another 30 insertions were conducted with a robot-assisted system under the same surgeons' supervision. We utilized a realistic, validated model of the temporal bone. This model accurately reproduces intracochlear frictional conditions and allows for the synchronous recording of forces on intracochlear structures, intracochlear pressure, and the position and deformation of the electrode array within the scala tympani. We identified a significant reduction in force variation during robot-assisted insertions compared to conventional procedures, with average values of 12 mN/s and 32 mN/s, respectively. Robotic assistance was also associated with a significant reduction in pressure peaks and a 17 dB reduction in intracochlear pressure levels. Furthermore, our study highlights that the release of the insertion tool represents a critical phase requiring surgical training. In conclusion, the motorized tool demonstrated more consistent insertion speeds compared to manual techniques. Its use can significantly reduce factors associated with intracochlear trauma, highlighting its potential for improved hearing preservation. However, it does not mitigate the impact of subsequent surgical steps like electrode cable routing and cochlear access sealing, pointing to areas in need of further research.

S2 L2 - Impact of Dexamethasone-Eluting Cochlear Implant Array on Longitudinal Electrode Impedance and Electrically Evoked Compound Action Potential Measures

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Introduction: Placement of a cochlear implant can be associated with intracochlear injury that can result in fibrotic scar formation and even stimulate ossification. Scar formation decreases the efficiency of electrical stimulation and can inhibit residual acoustic processing. Electrode impedance is sensitive to intracochlear fibrosis and increases over time post implantation. Dexamethasone has been shown to reduce scar formation and electrode impedance. Our center is evaluating subjects who have received dexamethasone-eluting electrodes as part of an ongoing prospective randomized multicenter trial and a non-randomized, single-center trial. The data reported here were collected as part of our NIH Clinical Research Center P50 Grant. A dense set of repeated impedance measures at time points shortly after surgery and repeated measures of access resistance and polarization impedance across the duration of implant use will be used to provide a detailed characterization of impedance changes across time. As dexamethasone also protects cochlear and neural function, electrically evoked compound action potentials (eCAP) are being evaluated to assess residual acoustic processing and efficiency of electrical stimulation over time.
Methods: Two separate populations of subjects have participated in this research. Eight of 9 cochlear implant recipients who participated in a randomized, double-blinded study to receive either a dexamethasone-eluting electrode array or a comparable, commercially available electrode array also participated in the P50 grant. 15 additional subjects have been implanted with a similar dexamethasone eluting electrode in the non-randomized arm of the study. Objective measures are performed at the time of surgery and at post-operative clinical visits. Electrode impedance is also assessed daily for 90 days post initial activation using a clinical smartphone app. Actual values and trajectories will be compared across groups and across intracochlear locations (e.g. basal vs apical electrodes).
Results: Preliminary analyses reveal that actual impedance values fall into one of two distinct ranges postoperatively. These results were expected and consistent with a previous study (Briggs et al., 2020). Impedance differences across groups were smallest at the time of surgery and increase post-operatively; this was true of total impedance as well as access resistance and polarization components. Impedance values increase most immediately following surgery and plateau; polarization impedance grows more steeply than access resistance, particularly at basal electrode sites. Descriptive patterns will be more formally assessed with inferential statistical analyses and comparisons will be made to the results reported by Briggs et al. (2020). The lower impedance values are associated with longer battery life. There

is a trend toward lower eCAP thresholds and steeper slopes for more apical electrodes compared to basal electrodes for both groups; group differences are not yet apparent. Analysis is ongoing.
Conclusion: Dexamethasone elution appears a promising strategy to reduce electrode impedance. It is of interest whether the impact will be observed in measures reflecting peripheral processing of acoustic and electric stimulation.

***S2 L3* - Unlocking the Cochlea with Synchrotron Phase-Contrast Imaging**

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Synchrotron Phase-Contrast Imaging (SR-PCI) has allowed for unparalleled three-dimensional views of the temporal bone. The spiral ganglion, basilar membrane, and peripheral axons were visualized and segmented. Ground truth angle-frequency measurements were made, and using an approach designed to minimize perceptual error in frequency estimation, an individualized frequency function was determined to relate angular depth to frequency within the cochlea. Novel artificial intelligence strategies were then employed to automatically segment the cochlea, determine total angular length, and frequency map individual cochlear implant electrode contacts. This patient-specific cochlear implant pitch-mapping has now been translated into patient care through pilot studies and planned randomized controlled trials.

S2 L4 - A Seamless Approach to EAS and Conventional Cochlear Implantation

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Until now, cochlear implantation (CI) has been broadly divided into conventional CI for patients with no residual hearing and electric-acoustic stimulation (EAS) for patients with residual hearing. EAS has been established as a standard treatment for patients with high-frequency hearing loss. However, it should be noted that high-frequency hearing loss is more or less progressive, with almost all candidates for EAS showing a progression of hearing loss of around 2dB/year (Okada et al., 2020). Further, there are many cases in which the hearing loss in an individual patient changes with time from being suitable for EAS to being suitable for conventional CI. Therefore, the natural course of hearing should be considered when selecting the most appropriate device for patients with residual hearing. In other words, it is necessary to formulate a treatment strategy that anticipates future audiograms, NOT treatment that considers current audiograms. Currently, as there are many borderline cases, it is actually difficult to draw a line between the indication criteria for these two interventions, and it has become necessary to consider the two as a single seamless approach.

Traditionally, EAS has been performed with relatively short electrodes of 24mm in length. On the other hand, a series of studies indicated that longer electrodes offered better speech perception compared with shorter ones. From this perspective, a complete solution is expected to require the use of longer electrodes to cover the entire cochlea (Yoshimura et al., 2020). To assess the benefit of EAS with long electrodes, we analyzed the results of hearing preservation (HP) and speech perception outcomes for EAS. A recent systematic review supports the view that longer electrodes provide higher HP rates in comparison to those observed for medium-length electrodes, thereby supporting our strategy (van de Heyning et al., 2022).

As it has been proven that residual hearing can be preserved even with long electrodes, opinion is changing toward the insertion of a long electrode appropriate to the size of the cochlea in patients eligible for EAS, regardless of the degree of residual hearing, and the utilization of that residual hearing after surgery.

Less invasive surgical techniques have been developed to preserve hearing in EAS, and the concept can be applied to conventional CI surgeries as well. As the concept of residual hearing preservation is based on the idea of protecting the auditory nerve (spiral ganglion cells), suppressing fibrosis and ossification within the cochlea, and preserving the structure of the inner ear, the basic concept has now evolved to apply to all CI surgeries, regardless of whether or not there is residual hearing. The concept of conventional CI and EAS as a single seamless approach is expected to be important in ensuring patients achieve their best performance outcomes.

S2 L5 - A Totally Implantable Cochlear Implant shows potential benefits for adults with hearing loss

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People with hearing impairment have several specific expectations: advanced technology providing superior outcomes, aesthetics, and reliability. The newly developed totally implantable cochlear implant (TICI) was designed to provide these. Advanced technology considers now and the future. Users experience benefits in speech understanding in quiet, speech understanding in noise, using the telephone, and listening to music. Aesthetics means having no visible audio processor, while still allowing a person to hear when they are in the shower, swimming, or when sleeping. Therefore, an increasing number of individuals with hearing loss might decide for cochlear implantation and enjoy the benefits thereof. A TICI comprises the housing and electrode of a conventional cochlear implant, while incorporating the microphone, the signal processing and the batteries previously contained in the external audio processor. A first-in-human clinical investigation using the MED-EL TICI system in six post-lingually deafened adults (21.3-73.2y) collected data over 52 weeks. The surgical procedure for the TICI is similar to the one used to implant currently marketed cochlear implants, except for the microphone positioning under the skin. Self-reported overall satisfaction was measured daily on a VAS scale. There was clear improvement from first fitting to 20 weeks. Monosyllable scores with the TICI improved from 6.3% pre-operatively to an average of 63.8% at 3-months post-operatively, further increasing to 70.3% at one year. The OLSA sentence test in noise determines the signal-noise ratio where 50% of sentences can be understood. No subject could complete the test pre-operatively. At 3-months post-operative, mean SRT with the TICI was -1.2 dB SNR and remained stable up to the one-year assessment. These scores were similar when comparing the TICI with the SONNET audio processor.The evaluation of the TICI in a first-in-human study, showed that expectations of users can be met. Surgeries were completed without incident. Speech-scores matched scores using an external audio processor. User satisfaction showed increasing satisfaction with the TICI over time. No unexpected safety events were recorded. The TICI shows the new way forward for cochlear implants.

S2 L6 - OCT imaging for atraumatic Cochlear implant surgery – CORLAS Vienna Meeting 2024

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Hypothesis: Optical coherence tomography allows for less traumatic cochlear implant (CI) insertion and for intracochlear diagnostics. Photon-counting CT imaging of the temporal bone allows for improved postoperative knowledge of CI electrode placement inside of the cochlea.
Background: In recent years, the planning of CI surgery has focused on the size of the cochlea and the orientation of the basal turn and hook region. The goal is to prepare the surgeon to minimize trauma during the insertion and to preserve the cochlear microstructures. Previous studies conducted by our group have evaluated the impact of localized insertional trauma on intracochlear tissue formation by virtually re-sectioning 3D reconstructions of the cochlea. Intra-operative navigation with a noninvasive imaging technique could open avenues for improved CI care. A postoperative assessment of the electrode placement would also be valuable for clinicians to predict long-term trauma and outcomes.
Methods: Pre- and postoperative images on Photon-counting CT images were retrospectively analyzed in CI subjects. Assessment of intracochlear electrode position was performed by an opensource software and verified with research software. Dislocation of the electrode array was assessed with the software, together with depth of insertion, and tonotopy. Proximity to the basilar membrane was also assessed. A visual inspection of CI imaging analysis of the scalae between the research software and the open-source software facilitated a detailed comparison. Feasibility studies have been conducted with OCT imaging from outside of the cochlea, as with an OCT fiber mounted on an insertion tool.
Results: Six cases were retrospectively analyzed. The software enabled the identification of the basilar membrane. Photon-counting CT imaging allows for adequate assessment of intracochlear electrodes. The detailed results will be discussed during the meeting. Relevant images of intracochlear tiny human microstructures will be shown and discussed in detail.
Conclusions: Photon-counting CT imaging allows for postoperative verification of electrode location. This retrospective analysis will facilitate the development of a more comprehensive prospective imaging protocol. Innovative basic research on OCT imaging outside and inside of the cochlea will allow for better intracochlear diagnostics and less traumatic CI surgery.

S3 L1 - Intracochlear electrocochleography: insight into speech perception with a cochlear implant

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Aim: To relate patterns of electrocochleography recorded across the cochlear implant electrode array during implantation to speech perception.
Methods: Electrocochleography was recorded directly from a slim lateral wall cochlear electrode at the end of implantation in patients with residual hearing of better than 90 dB at 500 Hz. In all patients, responses to 500 Hz acoustic stimuli were recorded, and also to 1000 or 2000 Hz stimuli when a response could be elicited. From these recordings the maximum amplitude of ECochG-derived waveforms (cochlear microphonic, auditory nerve neurophonic and summating potential) was determined, and the position (electrode number) on which this potential was observed. These summary characteristics of the ECochG were related to the patient's pre- and post-operative speech perception, using the statistical method of Generalised Additive Models (GAMs), as these allow for non-linear relations between variables to be modelled.
Results: In 113 recipients, the pre-operative audiometric thresholds were poorest when there was no recordable summating potential. Pre-operative thresholds were not significantly different in patients exhibiting positive or negative summating potentials. Pre-operative speech perception was significantly better when the summating potential was positive. In 110 patients, ECochG responses and post-operative hearing were related. GAMs explored the relationships between ECochG and the Consonant-Vowel-Consonant Phoneme (CVC-P) scores and Speech-Reception Thresholds in background noise at 3 and 12 months after implantation. For all measures, speech perception was significantly better than average when the summating potential was positive and poorer when negative, and speech perception was poorer when the summating potential was largest on the middle electrodes.
Discussion: One interpretation of these results is that inner hair cell responses are more robust in patients with a positive summating potential. In this case, both pre- and post- operative speech perception is better than average. This could potentially be attributed to improved inner hair cell survival providing better trophic support to the auditory nerve. We speculate that the poorer-than-average speech perception when the SP is on an electrode in the middle of the implant array is a consequence of contact between the electrode and the basilar membrane at this location. This may be expected to cause local trauma to the neural and sensory cells, and potentially reduce the function of the implant.

***S3 L2* - Assessment of cochlear nerve functionality in different vestibular schwannoma scenarios: insights gained for cochlear implantation**

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The use of cochlear implants (CI) is on the rise for patients with vestibular schwannoma (VS). Besides CI following tumor resection, new scenarios such as implantation in observed and/or irradiated tumors are becoming increasingly common. A significant emerging trend is the need of intraoperative evaluation of the functionality of the cochlear nerve in order to decide if a CI would be placed. The purpose of this study is to explore the experience of a tertiary center with the application of the Auditory Nerve Test System (ANTS) in various scenarios regarding VS patients. The results are compared to that of the studies that have previously used the ANTS in this condition.

Patients with unilateral or bilateral VS (NF2) who were evaluated with the ANTS prior to considering CI in a tertiary center between 2021 and 2023 were analyzed.
The presence of a robust wave V was chosen to define a positive electrical auditory brainstem response (EABR). Two patients underwent promontory stimulation (PromStim) EABR previous to ANTS evaluation.

Seven patients, 2 NF-2 and 5 with sporadic VS were included. The initial scenario was simultaneous translabyrinthine (TL) tumor resection and CI in 3 cases while a CI placement without tumor resection was planned in 4 cases. The ANTS was positive in 4 cases, negative in 2 cases, and uncertain in one case. Two patients underwent simultaneous TL and CI, 1 patient simultaneous TL and auditory brainstem implant, 3 patients posterior tympanotomy with CI, and 1 patient had no implant placement. In the 5 patients undergoing CI, sound detection was present.

There was a good correlation between the PromStim and ANTS EABR. The literature research yielded 35 patients with complete information about EABR response. There was one false negative and one false positive case; that is, the 28 implanted cases with a present wave V following tumor resection had some degree of auditory perception in all but one case.

The ANTS is a useful intraoperative tool to asses CI candidacy in VS patients undergoing observation, irradiation or surgery. A positive strongly predicts at least sound detection with the CI.

S3 L3 - Using focused thresholds to assess the electrode-neural interface in cochlear implants

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Objectives: In cochlear implants (CIs), the quality of the electrode-neural interface (ENI) is determined by the health of the surviving neural structures and their proximity to the electrodes. Absolute thresholds, measured via focused stimulation, have been used as an estimate of the ENI quality at individual electrodes. Here we tested two hypotheses related to the ENI: 1) Good ENI should be reflected not only by low absolute thresholds with focused stimulation, but also by narrow psychophysical tuning curves, indicating better spatial selectivity. 2) Focused stimulation should lead to narrower psychophysical spatial tuning curves than monopolar (MP) stimulation, particularly at locations with a good ENI.
Design: A total of 30 ears from 21 patients with the Advanced Bionics CI system were enrolled in this direct-stimulation study. Absolute thresholds were measured across the electrode array for each listener using focused stimulation (0.9-steered quadrupolar, sQP). The two electrodes with the highest and lowest focused thresholds were selected as target electrodes for measures of psychophysical tuning curves using forward masking. Both MP and 0.5-sQP stimulation modes for both masker and probe were used, with the test order of stimulation mode (MP or sQP) and electrode (low- or high-threshold) pseudorandomized.
Results: The variability of the thresholds across the array was found to be significantly smaller for the MP compared to the more focused sQP stimulation modes, as predicted. The dynamic range (DR) was not significantly different between the low- and high-threshold electrodes or between the two stimulation modes. Both the bandwidth and slopes of the spatial tuning curves were found to depend on stimulation mode (MP produced broader tuning then focused stimulation), but we found no significant effect of, or interaction with, the electrode threshold (low or high) on spatial tuning curves.
Conclusions: This study tested a larger number of ears than any previous detailed psychoacoustic study. We confirmed that focused stimulation leads to slightly but significantly better spatial resolution than MP stimulation. However, no systematic differences in tuning were observed between the low- and high-threshold electrodes, providing no support for our original hypothesis relating absolute thresholds to the quality of the ENI. The results support further investigation of the potential perceptual benefits of focused stimulation, but do not provide support for the approach of identifying better ENI and spatial selectivity through lower focused absolute thresholds. [Work supported by NIH grant R01 DC012262.]

***S3 L4* - Perioperative impedance measurements provide novel insights into the health and function of the cochlea after implantation: a prospective cohort study**

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Introduction: Residual hearing preservation is a good marker of cochlear health. The most reliable way to preserve it is through intraoperative monitoring of intracochlear electrocochleography (ECochG) and maintaining ECochG signal amplitude. Here, we test whether the prediction of hearing preservation can be improved by adding another biomarker: four-point impedance (4PI). 4PI measures the electrical conductivity near implant electrodes and is thought to reflect biological processes associated with implantation, such as inflammation and fibrosis. Both can impair residual hearing.

Methods: This was a prospective cohort study. Adults with residual acoustic hearing underwent cochlear implantation with intra-operative intracochlear electrocochleography (ECochG) monitoring. The surgeon responded to a drop in ECochG signal amplitude of >30% by a standardised electrode manipulation to restore the ECochG. At the end of the procedure, the ECochG signal was categorised as being maintained or having dropped more than 30%. 4PI was measured one day, one week, 1 and 3 months after cochlear implantation. The residual hearing was measured by routine pure-tone audiogram at three months post-operatively. The ECochG category and 4PI impedance values were entered as factors in a multiple linear regression predicting the protection of residual hearing.

Results: Twenty-six patients were recruited. ECochG significantly predicted residual hearing at three months (t-test, mean difference = 37.7%, p = .002). Inclusion of both 1-day or 3-month 4PI in a multiple linear regression with ECochG markedly improved upon correlations with residual hearing compared to the ECochG only model (rt-ECochG and 1-day 4PI model R2 = 0.67, rt-ECochG and 3-month 4PI model R2 = 0.72, ECochG only model R2 = 0.33).

Conclusions: Both ECochG and 4PI predict the preservation of residual hearing after cochlear implantation. These findings suggest that the biological response of the cochlea to implantation, as reflected in 4PI, is an important determinant of residual hearing, independent of the acute effects on hearing during implant surgery seen with ECochG. We speculate that this is because high inflammation one day after implantation and fibrosis at three months can impair cochlear function.

S3 L5 - Auditory Brainstem Implants: Are they Justified in Deaf Children with an Absent Cochlear-Nerve or Cochlea?

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Background: Auditory brainstem implants (ABI), directly stimulate the cochlear nucleus, bypassing the inner-ear and auditory-nerve. These implants may provide auditory benefit in a small group of deaf children who are not candidates for cochlear implantation (CI). Candidacy for ABI might include absence of the cochlear-nerve, cochlear aplasia or a non-implantable cochlea and patients who received but do not benefit from cochlear implantation. Because the auditory outcomes in children with ABI's are significantly inferior to those with CI's and are highly variable, some relevant professionals feel that the use of this technology may not be justified as the risk may exceed efficacy.

Objectives: To describe the outcomes in a series of children with ABI's treated in our University Medical Center, including the first ABI implanted nationally (2017), and demonstrate that in specific cases the technology is justified.

Methods: Of 12 patients with ABI's treated in Shaare Zedek Medical Center, 10 were children implanted between ages 2-8.6 years. Six boys and four girls. Six children had more than 2 years of follow up (2-7 years). Hearing evaluation was conducted, mainly, with audiograms, categories of auditory performance (CAP), speech perception testing when possible and hours of device use per day.

Results: Nine of the ten children, who initially underwent unsuccessful CI, had deficient auditory-nerves. One child had cochlear-aplasia. In 3 children hearing loss was related to CHARGE syndrome. CAP scores in the 6 children with sufficient follow up ranged from 0-7 (0,1,3,5,5,7). Four children identified all 6 ling sounds, 3 children were able to imitate them and one did not identify any sound. One child was able to achieve open-set speech perception and two others closed set. There were no significant medical/surgical complications from the surgery.

Conclusion: Although, functional auditory outcomes for children with ABI are highly variable and inferior to CI recipients, some of the children are able to obtain significant auditory benefit. We believe that in these children, ABI presents the only chance for auditory awareness and the use of the technology is safe and efficacious.

S3 L6 - Cochlear Implantation for Single-SidedDeafness in PediatricPatients: A Critical Assessment of Long-term Usage Rate

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Objective:
To assess the long-term usage rate of pediatric patients undergoing cochlear implantation (CI) for single-sided deafness (SSD) implanted in a tertiary care pediatric referralcenter

Methods:
Pediatric patients (age< 18 years-old) who underwent CI for SSD were included in the study. Each patient underwent a postoperative assessment including audiometric testing. The main outcome measures included device use and audiometric testing at last available visit up to two years post-implantation.

Results:
Sixty-six patients were implanted for SSD between 12/2018 and 7/2023 at a median age of 4.7-years-old (IQR 1.7-7.7). The cause of hearingloss was unknown in the majority of cases (27 patients, 41%) with cytomegalovirus being the most common known cause (17 patients, 26%). Hearing loss was pre-lingual in 38 patients (58%). Post-implantation, 12 patients (18%) were identified as lost to follow-up. For the remaining 54 patients, the median length of audiometric follow-up was 1.4 years (IQR 0.9-2.2). At last evaluation, only 10 of these 54 patients (19%) were designated as users (≥6 hours per day), and 13 patients (24%) were designated as limited users (>2 but <6 hours per day). Of patients capable of performing speech-in-noise testing (n=12), 10 patients (83%) showed improvement on BKB-SIN SNR-50 testing with their implant on versus off with a mean improvement of 3 dB. Notably, 3 of these 10 patients (30%) were categorized as non-users despite this benefit.

Conclusions:
Despite audiometric benefit from CI in the pediatric SSD population, long-term usage rate remains lower than anticipated at a high-volume, well-resourced tertiary pediatric center. Critical assessment is needed to identify trends for these findings to assure appropriate distribution of limited resources.

S4 L1 - Interferon signaling in the nasal epithelium distinguishes among lethal and common cold coronaviruses and mediates viral clearance

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All respiratory viruses establish primary infections in the nasal epithelium, where efficient innate immune induction may prevent dissemination to the lower airway and thus minimize pathogenesis. Human coronaviruses (HCoVs) cause a range of pathologies, but the host and viral determinants of disease during common cold versus lethal HCoV infections are poorly understood. We model the initial site of infection using primary nasal epithelial cells cultured at air-liquid interface (ALI). HCoV-229E, HCoV-NL63 and human rhinovirus-16 are common cold-associated viruses that exhibit unique features in this model: early induction of antiviral interferon (IFN) signaling, IFN-mediated viral clearance, and preferential replication at nasal airway temperature (33ºC) which confers muted host IFN responses. In contrast, lethal SARS-CoV-2 and MERS-CoV encode antagonist proteins that prevent IFN-mediated clearance in nasal cultures. Our study identifies features shared among common cold-associated viruses, highlighting nasal innate immune responses as predictive of infection outcomes and nasally directed IFNs as potential therapeutics.

S4 L2 - Drug Repositioning for Nasal Polyp Therapy: Effects of HMG-CoA Reductase Inhibitors on Fibrinolytic System Activity

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Background:
HMG-CoA reductase inhibitors are first-line agents for the treatment of hyperlipidemia, however, they are known to have a multiplicity of pharmacological properties. They promote the production of tPA (tissue plasminogen activator) from vascular endothelial cells and have an inhibitory effect on cardiovascular disease due to their fibrinolytic activity (Kruithof et al. Thromb Haemost. 2014). Epidemiologic data reported that oral administration of statins has a preventive effect on sinusitis (Wilson et al. Laryngoscope. 2020, Gilani et al. Laryngoscope. 2021).

Objective:
To elucidate the effect of HMG-CoA reductase inhibitors on the activity of the fibrinolytic system.
Methods: In human normal airway cells (NHBE), mRNA and protein expression of tPA were measured after stimulation with HMG-CoA reductase inhibitor (Fluvastatin) for 24 and 48 hours. In addition, mRNA and protein expression of tPA were measured by co-stimulation of tPA with IL-13, an inhibitory cytokine of tPA.
Results:
After stimulation with fluvastatin for 24 hours, tPA mRNA expression showed a concentration-dependent increase. The results of a comparative study of the effects of other reagents are reported.

Discussion:
Statins are one of the most widely prescribed drugs in the world, and their clinical safety has been demonstrated. In the present study, we investigated the fibrinolytic activity of statins, one of their multiple pharmacological actions, and found that they may antagonize the suppression of tPA production by type 2 inflammation associated with chronic sinusitis. Therefore, as a position in the treatment of sinusitis, it is expected to be useful in drug repositioning application for prevention of postoperative recurrence.

Conclusion:
Statins are widely used drugs in general, and their use for nasal polyp control in chronic sinusitis is suggested to be useful.

S4 L3 - Murine model of eosinophilic chronic rhinosinusitis using topical application of vitamin D3 analogue

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Background:
Eosinophilic chronic rhinosinusitis (ECRS) is a chronic inflammatory disease, characterized by eosinophilic infiltration, T-helper type 2 (Th2-type) response, and olfactory disfunction. Thymic stromal lymphopoietin (TSLP) is a master regulator of Th2-type inflammation and important for basophil activation. TSLP-elicited basophil is a key factor of the pathogenesis of ECRS.

Methods:
In order to elucidate the mechanisms of ECRS in humans, we aimed to establish a murine model of ECRS, based on TSLP production by topical application of MC903 (analogue of vitamin D3) and TSLP-induced basophil activation. The infiltration of immune cells in the nasal mucosa was assessed by histology. The status of Th2-type inflammation was evaluated by quantitative real-time PCR. The impact of eosinophilic inflammation on the olfactory epithelium was evaluated by histology.

Results:
In the mice treated with MC903 and ovalbumin (OVA), eosinophils, basophils, and macrophages were increased in the nasal mucosa, compared to those treated with OVA alone or the controls. Quantitative real-time PCR revealed elevated expression of interleukin (IL)-4, IL-5, IL-13, TSLP, chemokine CCL11, and CCL24 in the nasal mucosa of the ECRS model. In parallel, the thinned olfactory epithelium and decreased mature olfactory sensory neurons were observed in the ECRS model.

Conclusions:
Our mouse model of ECRS displayed a Th2-type inflammation in the sinonasal region, including both eosinophil and basophil infiltration. Additionally, eosinophilic inflammation had impact on the olfactory epithelium. These features are consistent with the characteristic of human ECRS.

S4 L4 - Pediatric endonasal endoscopic skull base surgery: Long-term impact on sino-nasal outcome, olfaction, and facial development

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Objective: Endonasal endoscopic skull base surgery (EESBS) gradually became one of the standard approaches for addressing various lesions along the anterior and central skull base in the adult but also pediatric populations. Despite important advantages that endonasal approaches enable in favor of patients, potential negative effects in pediatric patients in long term are not completely understood. Our aim is to investigate how sino-nasal outcome, olfactory function, and facial development are being affected in pediatric patients after EESBS in the long term.

Methods: The records of pediatric patients who underwent EESBS from 2012 to 2022 and had regular follow-up visits were retrospectively and prospectively analyzed. Sino-Nasal Outcome Test 22 (SNOT-22) questionary and Extended Sniffin' Sticks Test (including Identification, Discrimination and Threshold scores) were used respectively to assess impact of severity of sino-nasal symptoms and status of olfaction years after surgery, which were compared with the data of a healthy control group. All patients had magnetic resonance imaging (MRI) and computed tomography (CT) with the jaws fully closed at the individual's longest follow-up term which were used to measure facial growth from points (S:sellar, N:nasion, B:supramental and A:subspinal) and angulations (SNA, SNB and ANB) used in Bolton standards for facial development evaluation and compared with a healthy control group. Additionally, preoperative and postoperative hormone levels were also checked and recorded.

Results: A total of 30 patients, 19 (63.3%) boys and 11 (36.7%) girls were included in this study, whose mean age at the time of surgery was 10.23±5.00 years and current mean age was 15.97±5.45 years with a mean follow-up time of 6.73±2.01 years. In 23 (76,66%) cases surgery was performed for a sellar-suprasellar pathology. Panhypopituitarism developed preoperatively in 5 patients and postoperatively in 6 patients. Pedicled flaps were used in 24 patients for defect closure. Mean SNOT-22 score was 10.37±10.83 compared to 9.59±8.68 in the control group showing no statistically significance regarding the impact of sinonasal symptoms on quality of life. Mean odor total score was 33.92±2.98 and when compared with the control group no statistically significant difference was found in olfactory function in terms of age and gender, p=0.928 and p=0.584, respectively. In

the mean follow-up of 7 years, 86.7% of the cases had normosmia and no functional anosmia. As for facial development no statistically significant difference was observed between the cases and gender specific standard averages as well as control group in terms of SNA, SNB, and ANB angulation measurements on radiological imaging. ($p > 0.05$).

Conclusion: Our findings reveal no statistically significant negative impact of EESBS on sino-nasal quality-of-life outcome, olfactory function and facial development in the pediatric age group compared to an age and gender matched control group at a mean follow-up of 7 years after surgery. Endoscopic approaches to the skull base seem to protect facial growth and sino-nasal function of the developing child in the long-term and can safely be utilized.

S4 L5 - The Role of Surgery in Orbitocranial Fungal Infection Treatment in the Era of Azole Antifungals

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Introduction:
Aggressive surgery has been justified in orbitocranial fungal infection (OCFI) as life-saving, despite its significant morbidity and the long-term effect on survivors' life quality. Over the past two decades, early use of azole agents has been introduced as a first-line treatment, demonstrating promising outcomes. However, to date, there is no data regarding the contribution of surgery in the "azole era" to patients' survival. This work aimed to provide real-life data on azole treatment outcomes and the role of surgery in the current management of OCFI.

Methods:
Data was collected retrospectively from a chart review from four participating centers and a systematic literature review. The study group included patients with OCFI treated with azole antifungals. The control cases were treated with other antifungal agents. The degree of cranial and orbital involvement was staged based on the imaging. The extent of the surgical resection was also classified to allow for inter-group comparison.

Results:
There were 125 patients in the azole-treated group and 153 in the control group. Among the patients with OCFI cranial extension, 23% were operated on in the azole-treated group and 18% in the control group. However, meninges and brain resection were performed only in the controls (11% of patients) and never in the azole antifungals group (p-value=0.045). Orbital involvement required surgery in 26% of azole-treated cases and 39% of controls. Despite a more aggressive cranial involvement (p-value<0.01), azole-treated patients' mortality was significantly lower than in controls, with an OCFI-specific mortality rate of 21% vs. 52%. A similar trend was found for the extent of the orbital disease and the orbital surgery.

***S4 L6* - Treatment of dilatory Eustachian tube dysfunction: From balloon dilation to absorbable stent and results of a randomized multicenter study**

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Background: Balloon eustachian tuboplasty (BET) has emerged as a new treatment modality for dilatory eustachian tube (ET) dysfunction and resulted in significant improvement of symptoms in several studies. However, only a few studies have been reported about BET in patients with chronic otitis media (COM). We aimed to assess the efficacy and safety of BET in comparison with medical management (MM) alone in adult patients with COM accompanied by dilatory ET dysfunction. For failure cases after BET, various preclinical studies with developed ET stents are in progress but have not yet been clinically applied. Use of ET stent is limited by stent-induced tissue hyperplasia in preclinical studies. Thus, we evaluated the tissue reaction to absorbable magnesium stents for future clinical use.
Materials and Methods: This prospective, multicenter, randomized controlled trial included 122 participants (128 ears) with ET dysfunction from January 2021 to June 2023 at three tertiary centers in South Korea. Participants were randomized BET plus MM or MM alone. Dilatory ET dysfunction was defined as the negative Valsalva maneuver and the effectiveness of BET was the successful Valsalva maneuver. The short-term primary effectiveness endpoints were analyzed at 8-week follow-up.
Results: A total of 128 ears were assigned to BET group (68 ears) and control group (60 ears) with MM alone. In BET group, 47.1% (32/68) had positive Valsalva maneuver, while only 16.7% (10/60) showed positive Valsalva maneuver in control group ($p < 0.001$). Regarding change of total ETDQ-7 scores, participants in BET group (-6.87 ± 9.36) had much more improvement in symptoms than those in the control group (-2.68 ± 8.56, $p < 0.001$). ABG was significantly decreased after the procedure in the BET group (-6.26 ± 11.64 dB HL, $p < 0.001$) compared to the control group (-1.15 ± 10.37 dB HL, $p = 0.396$). No procedure-related or device-related serious adverse event was reported through the 8-week follow-up in either the BET group or the control group.
Conclusions: In dilatory ET dysfunction accompanied with COM, BET in conjunction with MM has superiority compared to MM alone. BET leads to a significant positive Valsalva maneuver and reduction in the mean overall ETDQ-7 scores and ABG compared to the control group. BET is a safe, effective treatment for chronic dilatory ET dysfunction which is supposed to cause COM. For failure cases, a drug-coated stent might be effective in suppressing stent-induced tissue hyperplasia in porcine model. However, further investigation was required to verify the optimal stent materials and antiproliferative drugs.

S5 L1 - Transmastoid two-point plugging of superior semicircular dehiscence with preservation of vestibulo-ocular reflex

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Introduction:
In the treatment of superior canal dehiscence syndrome (SCDS) by means of transmastoid plugging, a loss of function of the vestibular ocular reflex (VOR) of the this semicircular canal would usually be expected, as the endolymph flow in the semicircular canal is disturbed by the plugged semicircular canal during rotational accelerations.

Method:
In this mixed retrospective and prospective case series, ten patients with typical clinical symptoms and radiological and functional diagnostic (4 kHz oVEMPs) proof of the SCDS were surgically treated by means of transmastoid two-point plugging of the canal. The superior semicircular canal was opened anterior and posterior to the dehiscence and the canal was blocked with connective tissue and Bone pâté. Video head impulse test (vHIT) was used to evaluate the VOR preoperatively and postoperatively.

Results:
All patients experienced a significant reduction in the symptoms or even a symptom-free situation. Interestingly, despite blocking of the superior semicircular canal, the VOR was preserved with normal gain and absence of correcting saccades.

Discussion:
One possible explanation could be the deformability of the endolymphatic tube, which has been described in animal experiments in particular at high stimulation frequencies, which can lead to endolymphatic movements in the area of the ampulla with deflection of the cupula despite blocking of the semicircular canal.

S5 L2 - Impact of Vibrations and Rapid Decelerations on SemontPLUS Maneuver Efficacy: An In Vitro Study

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Objective:
We aim to investigate the effect of adding 'rapid decelerations' and 'vibration' during a SemontPLUS maneuver on the dynamics of the inner ear and the success rate of canalolithiasis repositioning.

Methods:
We used a previously described upscaled (x5) in Vitro model of the posterior semi-circular canal of the inner ear to analyze the trajectory of a 'single' and 'clumped' surrogate otolith particle (metallic sphere) during an SemontPLUS maneuver (-60° below earth horizontal) on a repositioning chair (TRV). We compared the angular displacement, the velocity and acceleration of these particles with and without the application of vibration or rapid decelerations using TRV. We recorded the success rates of the SemontPLUS maneuver for each condition.

Results:
After the first step of the SemontPLUS, the application of vibration increased the angular displacement of single particles from 119.9° to 125.4° and clumps from 108.4° to 123.8°. Clumps travelled shorter distances than single particles. Rapid decelerations also increased the angular displacement from 119.9° to 124.6° and 108.4° to 113.6° for singles and clumps, respectively. Vibration and rapid decelerations applied on the in Vitro model resulted in enhanced repositioning success rates to 73% in both conditions.

Conclusions:
Adding rapid decelerations or vibration to the SemontPLUS maneuver increased otolith particle displacement and improved the repositioning success rates in an in-Vitro model. An enhanced SemontPLUS maneuver (adding vibratory stimulation or rapid decelerations) has the potential to improve outcomes, provided that future clinical trials confirm its efficacy.

S5 L3 - Digitally assisted sensorimotor brain stimulation for the therapy of Vertigo

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Sensorimotor exercises are a classic method for treating dizziness. These lead to brain stimulation, the repetition of which leads to a learning process that triggers cerebral vertigo compensation. To facilitate this treatment, we have digitized sensorimotor exercises and combined them in a Digital Therapeutic (DTx, name: Vertidisan). With the Vertidisan DTx, the patient performs sensorimotor exercises for 10-20 minutes every day for 90 days. A confirmatory, group-controlled, randomized clinical trial Sensorimotor exercises are a classic method for treating dizziness. These lead to brain stimulation, the repetition of which leads to a learning process that triggers cerebral vertigo compensation. To facilitate this treatment, we have digitized sensorimotor exercises and combined them in a Digital Therapeutic (Vertidisan DiGA). With the Vertidisan DiGA, the patient performs sensorimotor exercises for 10-20 minutes every day for 90 days. We run a confirmatory, group-controlled, randomized clinical trial. Among the DiGA users, 87.73% were responders, with a statistically significant average vertigo reduction of −76.15% ($p < 0.0001$) while in the control (physiotherapy) group, only 25.47% were responders (rate difference 62.3%; 95% CI, 51.9% to 72.6%; $P<0.0001$). The confirmatory group comparison revealed a highly significant (adjusted LSMean -7.9 score points, 95% confidence interval -9.5 to -6.2 score points, $p<0.0001$; Cohen's d: 1.55) treatment effect of the DiGA. This finding was supported by a series of further confirmatory group comparisons—including vertigo handicap, improvement, severity, and distress—all of which showed similar significant superiority of the DiGA group vs. the control group ($p < 0.0001$). Thus, the Vertidisan DiGA effectively resulted in a significant reduction or even remission of vertigo, showing efficacy that was significantly superior to physiotherapy. The data from this randomized controlled trial reveal a substantial benefit of the DiGA for patients suffering from peripheral vertigo.

S5 L4 - Virtual Reality in Vestibular Assessment

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Introduction:
Dizziness is a common complaint affecting up to 23% of the world population. Diagnosis is of utmost importance and routinely involves several tests to be performed in specialized Centers. The advent of a new generation of technical devices would make envision their use for a valid and objective vestibular assessment. Microsoft HoloLens 2 (HL2) Mixed Reality headset has the potential to be a valuable wearable technology that provides interactive digital stimuli and inertial measurement units (IMUs) to objectively quantify the movements of the user in response to various exercises.

Objective:
The aim of this study was to validate the integration of HoloLens with traditional methods used to analyze the vestibular function in order to obtain precise diagnostic values in normal and pathological populations.

Methods:
Twenty-six healthy adults completed the Dynamic Gait Index (DGI) tests both with a traditional evaluation and while wearing HL2 headset, thus allowing to collect kinematic data of normal patients' head and eyes. The subjects had to perform 8 different tasks and the scores were independently assigned by two Otolaryngology specialists. Similar examination also involved a group of patients affected by Ménière's disease. Platform stability and subjective visual vertical (SVV) were also investigated. A robust statistical support was also provided.

Results:
The maximum of the mean position of the walking axis of the subjects was found in the DGI second task (-0,14±0,23 m), while the maximum value of the standard deviation of the walking axis was found in the fifth task (-0,12±0,27 m). No statistical differences were found for DGI in Menieric patients who instead showed divergent data when analyzed for SVV test.

Conclusion:
The mixed reality applied to vestibular testing showed promising results that need confirmation by applying it to a broader sample of patients with different vestibular disorders.

***S5 L5* - Effects of Meniere's treatments on vertigo frequency and endolymphatic space volume evaluated by using inner ear MRI**

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Nowadays, the endolymphatic space size can be evaluated by 3D-analysis of 3T-MRI after intravenous injection of gadolinium enhancement. In the present study, to elucidate the relationships between vertigo and endolymphatic hydrops (EH) volume after pressure pulse treatment (PPT), we investigated changes in EH volume after PPT for intractable Meniere's disease (MD) by means of the inner ear MRI (ieMRI) in relation to clinical results. Ninety patients completed the planned 2-year-follow-up, which included assessment of vertigo frequency and changes in EH volume using ieMRI (PPT: n=40; endolymphatic sac drainage (ELSD): n=50). Two years after treatments, vertigo was completely controlled in 77.5% of patients in PPT and 90.0% in ELSD. Hearing improved by >10 dB in 7.5% in PPT and 24.0% in ELSD. EH volume was significantly reduced after treatments of PPT and ELSD only in the vestibule. The obtained results indicate that PPT as well as ELSD could be a good treatment option for patients with intractable MD.

S5 L6 - Vestibular schwannoma management in the 21st century- emotional and other investments in decision making?

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The management of patients presenting with a vestibular schwannoma has evolved over recent decades and the evidence base underpinning this has accrued.

This presentation firstly presents some historic context and then the author's decision making based on a prospectively collected series over 3 decades. This is then contextualised within the British Skullbase Society National Vestibular Schwanomma Audit which comprises over 18,000 cases and contemporary literature.

Based on the current evidence base the author asks the questions as to whether there are emotional and other investments in decision making?

S6 L1 - Assessment and Time-Frequency Analysis for Gait Patterns Recognition in Unstable Older Patients with Vestibular Hypofunction

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Background:
Gait instability and falls exert a considerable negative influence on the quality of life and morbidity/mortality rates among elderly populations. Diminished sensory input associated with bilateral vestibular hypofunction often cited as a contributing mechanism to instability in this demographic.

Objective:
This study aims to find a gait instability pattern in older adults with bilateral vestibular hypofunction by employing image representations of data gathered from a single sensor.

Methods:
A cohort comprising 13 older adults (aged 71-85) exhibiting instability due to Vestibular Hypofunction (VH) was compared to a control group of eight older adults (aged 70-75) with normal vestibular function and no instability. Utilizing a continuous wavelet transform (CWT) of specific dataset components, image representations of gait signals captured along a predetermined walking path were generated. These images were analyzed as textures employing grey-level co-occurrence matrix metrics as features. A support vector machine (SVM) algorithm was deployed to differentiate between the two subject groups, employing a ten-fold cross-validation technique applied to the initial ten seconds of the dataset.

Results:
The analysis yielded a robust classification performance on the collected data. Notably, the mediolateral acceleration (X-axis) and frontal plane angular rotation (Z-axis gyroscope) were identified as containing sufficient discriminatory information for effective classification. The algorithm achieved a 96.3 F1 score, corresponding to 13 true positives, one false positive, and no false negatives.

Conclusions:
This study suggests that the proposed methodology holds promise for assessing gait disorders, particularly in uncontrolled environments. Moreover, it implies the potential applicability of convolutional neural networks for automatic pattern assessment of gait stability across diverse environmental conditions.

S6 L2 - Hearing and Vestibular Manifestations in Fabry Disease Patients: A Cross-Sectional Study in Taiwan

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Background: Fabry disease (FD) is a genetic disorder characterized by systemic accumulation of globotriaosylceramide (Gb3), leading to multi-organ pathology. While its cardiovascular and neurological implications are well-documented, the potential auditory and vestibular manifestations remain under-explored. This study aimed to determine the prevalence and severity of auditory, tinnitus, and balance function abnormalities in FD patients.

Methods: A cross-sectional study was conducted from January 2022 to December 2023 at Taipei Veterans General Hospital. The study included 112 FD patients with a median age of 64.3 years (range: 17.9 to 80.0 years, SD: 12.6). Participants were classified into three groups based on their genotypes: classic, cardiac, and others. Otologic assessments included pure tone audiometry and balance function tests.

Results: Among the 112 participants, 58.5% were male and 41.5% were female. Hearing thresholds increased with frequency, peaking at 34.9 dB HL at 4000 Hz and 42.8 dB HL at 8000 Hz. One participant did not undergo pure tone audiometry, and five did not disclose their tinnitus history. In the cardiac variant group, 81.5% experienced hearing loss, 59.8% reported tinnitus, 42.0% had a high-tone loss, and 34.6% had hearing asymmetry. Distortion product otoacoustic emissions (DPOAE) showed a lack of response in 50.8% of tested ears. In the classic and other variants, 66.7% exhibited hearing loss. Tinnitus was noted in 72.2% (classic) and 58.3% (other), with hearing asymmetry in 38.9% (classic) and 33.3% (other). High-tone loss was found in 44.4% (classic) and 50.0% (other). Lack of DPOAE response was evident in 76.9% (classic) and 77.8% (other) of tested ears. Vestibular function abnormalities were evident in 80.6% of the cohort.

Conclusions: This study highlights the necessity of incorporating audiological and vestibular evaluations into the multidisciplinary assessment of FD patients in Taiwan. FD is significantly associated with specific auditory manifestations, including hearing loss, sudden deafness, and tinnitus. Healthcare providers managing FD patients should remain vigilant about these potential otologic manifestations, and routine otologic consultations are imperative. Future research is essential to explore the underlying mechanisms of these otologic comorbidities in FD.

S6 L3 - Respiration-synchronized Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea: Historical background and Belgian results from the ADHERE registry

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Historical Background and Rationale: Respiration-synchronized hypoglossal nerve stimulation (HGNS) has emerged as a widespread innovative treatment option for selected moderate to severe obstructive sleep apnea (OSA) patients who cannot be effectively treated with continuous positive airway pressure or mandibular advancement device therapy. A first-ever in-men implantation of a 1 st generation HGNS system was successfully performed at the Antwerp University Hospital (UZA) in Belgium in 1996. In the pilot study evaluating the 2 nd generation HGNS systems (Inspire Medical Systems, Minneapolis, MN, USA) the authors could illustrate that patients with body mass index (BMI) < 35 kg/m2 , apnea/hypopnea-index (AHI) between 15 - 65/hour sleep, and/or absence of complete circular collapse during drug-induced sleep endoscopy are more likely to be HGNS responders (Van de Heyning et al. 2012). The research team at UZA participates in the ADHERE registry, a global observational study collecting data from OSA patients receiving HGNS therapy in routine clinical care. In this abstract, an analysis is performed on the ADHERE registry outcomes of the first series of Belgian OSA patients treated with respiration-synchronized HGNS.

Methods: Consecutive patients that received an Inspire HGNS implant at UZA were prospectively included in the ADHERE registry. The registry collects data from different clinical visits: preimplant, implant, post-titration 6 months post-implantation and after 1-year. Several outcomes of HGNS therapy were collected during the post-implantation follow-up, including AHI, Epworth sleepiness scale (ESS), therapy usage and patient satisfaction. Surgical success was defined according to the Sher criteria: a reduction in baseline AHI of more than 50%, and a postoperative AHI of less than 20 events/h. Questionnaires on patient satisfaction and the ESS were filled out at baseline and during the follow-up visits. Objective therapy usage was retrieved from data stored in the implantable pulse generator. A non-parametric paired Wilcoxon signed-rank test was used to compare pre-implant data with follow-up data. Data are presented as median [quartile 1, quartile 3].

Results: In total, up to date, 44 Belgian patientsreceiving an Inspire implant (age 54.7±11.9 (mean±SD) years, male 80%, BMI 27.6±2.9 kg/m2 , AHI 35.3 [25.6-45.2] events/h) are included in the ADHERE registry. Thus far, 36 patients have completed the post-titration follow-up. Median AHI was reduced from 32.7 [25.6-45.2] events/h

to 9.1 [4.3-19.7] events/h post-titration (p<0.001). Surgical success rate according to the Sher criteria was 83% at the this follow-up. Median ESS improved from 12 [7-18] pre-implant to 5 [2-11] post-titration (n=29; p<0.001). Therapy usage post-titration was 7.4 [6.3-8] hours/night (n=36). At the post-titration follow-up, 100% of the patients state that HGNS was better than CPAP therapy, 100% would choose HGNS therapy again, 100% would recommend HGNS therapy to friends/family and 100% were satisfied with HGNS therapy. Up till now, 1-year follow-up data is available from 13 patients. Surgical success rate according to the Sher criteria was 84.6% and therapy usage follow-up was 7 [5.9-9.1] hours/night, both at the 1-year follow-up.

Conclusion: This preliminary analysis of Belgian patientsincluded in the ADHERE registry shows significant improvement in both objective and subjective OSA outcomes under HGNS therapy with a high patients' satisfaction and high therapy adherence.

S6 L4 - A Comparative Study of 11 Wearable, Nearable, and Airable Consumer SleepTrackers

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Background: Consumer sleep trackers (CSTs) have gained significant popularity, because they enabled individuals to conveniently monitor and analyze their sleep. However, limited studies have comprehensively validated the performance of widely used CSTs. Our study therefore investigated popular CSTs, which based on various biosignals and algorithms by assessing the agreement with polysomnography.

Objective: This study aims to validate the accuracy of various types of CSTs through a comparison with PSG. Additionally, by including widely used CSTs and conducting a multicenter study with a large sample size, there search seeks to provide comprehensive insights into the performance and applicability of these CSTs for sleep monitoring.

Methods: The study analyzed 11 commercially available CSTs including five Wearables (Google Pixel Watch, Galaxy Watch 5, Fitbit Sense 2, Apple Watch 8, and Oura Ring 3), three Nearables (WithingsSleep Tracking Mat, Google Nest Hub 2, and Amazon Halo Rise), and three Airables (SleepRoutine, SleepScore, andPillow). The 11 CSTs were divided into two groups, ensuring maximum inclusion while avoiding interference between the CSTs within each group. Each group (comprising 8 CSTs) was also compared via polysomnography.

Results: The study enrolled 75 participants from a tertiary hospital and a primary sleep-specialized clinic in Korea. Across two centers, we collected a total 3890 hours of sleepsessions based on the 11 CSTs along with 543 hours of PSG recordings at the two centers. Each CST sleep recording covered an average of 353 hours. We analyzed a total of 349,114 epochs from the 11 CSTs compared with PSG, where epoch-by-epoch agreement in sleep stage classification showed substantial performance variation. More specifically, the high estmacro f1 score was 0.69, while the low estmacro f1 score was 0.26.

Conclusions: Our study showed that among the 11 CSTs examined, specific CSTs showed substantial agreement with PSG, indicating their potential application in sleepmonitoring, while other CSTs were partially consistent with PSG. This study offers insights into the strengths of each CST within the three different classes.

S6 L5 - Exploring temporal dynamics of subjective impairment and objective/subjective olfactory function in a cohort study of 524 patients

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Objective: It has long been known that subjective self-assessment of olfactory ability is unreliable even though it has never been examined whether the reliability of self-assessment improves over time. Moreover, it can be assumed that self-assessment of olfactory function is associated to the subjective impairment caused by the olfactory disorder. We aimed to investigate changes in self-assessment and subjective impairment over time and possible associations between subjective assessment/impairment and objective measurement.
Methods: 524 patients (median age, 54 y; range, 15-88 y, 265 females and 259 males) seeking advice in our smell and taste clinic were examined two or more times. Prior to psychophysical testing subjective impairment was evaluated in all patients using a visual analogue scale (VAS) ranging from 0 (no impairment) to 10 (very intense impairment). Subjective olfactory function (each identification and discrimination) was evaluated with a VAS (0-10): Zero was considered no olfactory function/ discrimination ability and 10 a perfect olfactory function/discrimination ability. Endonasal endoscopy and olfactory testing (lateralized Sniffin' Sticks) were performed in all patients and olfactory disorder classified according to history, endonasal findings and results of the Sniffin' Sticks test (TDI score, composite score of Threshold, Discrimination and Identification). We analyzed subjective impairment and subjective olfactory function over time with generalized linear models—accounting for patient-level confounders and within-patient clustering (random intercepts).
Results: 1,201 examinations were performed in 524 patients (382 [73%] were examined twice, 123 [23%] three times; overall range, 2-6 exams). The median time interval between the event and first examination and first and last examination was 9 months (interquartile range [IQR], 5-14) and 11 months (IQR, 8-21), respectively. The most important diagnoses were posttraumatic (34%), postinfectious (29%) and other (31%) disorders besides sinonasal and neurodegenerative disorders. Overall, subjective impairment decreased significantly over time (adjusted p<.001) from a median of 9 (IQR, 6-10) to 7 (IQR, 4.5-9.5), subjective assessment of olfactory function increased from a median of 0.5 (IQR, 0-2.5) on VAS to 1.2 (IQR, 0-4; adjusted p=.001), psychophysical olfactory function improved as well, mostly pronounced in the postinfectious group. Subjective impairment and subjective olfactory measures were significantly associated with TDI scores (adjusted p<.001).
Conclusion: Subjective impairment caused by olfactory disorders decreases significantly over time, independent of objective measurements, even if subjective olfactory ability improves only slightly—but significantly as well. Coping mechanism seem to be effective to reduce subjective impairment.

S6 L6 - The role of MRI in post-traumatic olfactory dysfunction

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Background:
Although most patients with post-traumatic olfactory dysfunction (PTOD) undergo MRI, there is no consensus about its diagnostic or prognostic value. The aims were: (1) to classify the extent of post-traumatic neurodegeneration; (2) to determine its relationship with chemosensory dysfunction (smell, taste, trigeminal); and (3) to establish whether MRI can predict olfactory improvement.

Methodology:
We conducted a retrospective cohort study based on a series of 56 patients with PTOD. All patients underwent validated psychophysical tests of their smell, taste, and trigeminal functions, otorhinolaryngologic evaluation, and MRI. An experienced radiologist blinded to patient data evaluated 40 chemosensory-relevant brain regions according to a four-point scale (0=no lesion to 3=large lesion). Follow up data after 4 years (on average) were available in 46 patients.

Results:
The cluster analysis showed 4 brain lesion patterns that differed in lesion localization and severity. They are associated with diagnostic categories: anosmia, hyposmia and normosmia. Two clusters were highly specific for anosmia (100% specificity) and could accurately predict this condition (100% positive predictive value). No clusters were associated with trigeminal or taste dysfunction. Regarding improvement, 72.7% of patients in the cluster with mild lesions experienced subjective and measurable olfactory improvement whereas this was only the case in 21.7-37.5% of patients with larger lesions. The odds of subjective smell improvement were 5.9 times higher in patients within the milder cluster compared to larger ones.

Conclusions:
The analysis of brain lesions in PTOD allows corroboration of smell test results and prediction of subjective and measurable improvement.

S6 L7 - Complex nasal reconstruction using forehead flap prelamination and 4D-CT angiography

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Introduction:
The paramedian forehead flap is the workhorse for the reconstruction of complex and multilayered nasal defects. The presence of a patent supratrochlear artery is vital for sufficient blood supply of such flaps. In this study we demonstrated, that 4D-CT angiography is a valuable tool for surgical planning. Flap prelamination with or without tissue expansion is applied for different reconstructive purposes.

Material and Methods:
In this study, complex nasal defects involved large skin defects, defects of skin and cartilage as well as three-layered defects affecting at least one anatomical subunit. Preoperatively, sixteen patients underwent dynamic 4D-CT angiography (CTA) (Somaton Force, Siemens, Healthineers) to evaluate blood supply of the forehead. Prelamination with split skin grafts from the thigh was applied in six patients with large three-layered defects and combined with flap expansion in one patient.

Results:
Perfusion of the supraorbital plexus and the supratrochlear artery could be visualized in 15 out of 16 patients. These data were then integrated and used for preoperative planning. Prelamination with split skin grafts is technically relatively easy and can be combined with flap expansion if needed. Integrity of the internal, prelaminated layer was impaired in one patient who did not quit smoking.

Conclusions:
Advanced techniques such as dynamic 4D-CTA or prelamination of forehead flaps can improve preoperative decision making and surgical planning in the complex reconstruction of multilayer defects. Prelamination is mainly used in large three-layered defects, when other options for the reconstruction of the internal lining, such as composite grafts or other skin flaps don´t seem feasible.

S7 L1 - Precision Medicine and Gene Therapy for Hearing Loss and Vestibular Dysfunction

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Precision medicine is an emerging concept, allowing for early diagnosis and precise treatments. The field of hearing loss is ideal for applying a precision medicine approach, since it is genotypically and phenotypically heterogeneous, with close to 200 deafness-related genes identified to date. The shift to precision medicine is supported by the integration of next generation sequencing (NGS), which has facilitated rapid variant identification and gene discovery. Therapeutic strategies, such as biological treatments, are becoming increasingly relevant for treating genetic hearing loss. Thus far, successes have been made for otoferlin-related autosomal recessive deafness in clinical trials in humans. To demonstrate proof of principle for an adeno-associated virus (AAV)-based precision medicine approach, we explored rescuing hearing in Clic5 mutant mice, a model of human hearing loss. CLIC5 is encoded by the Chloride Intracellular Channel 5, part of the family of chloride ion channels, and is associated with actin-based cytoskeletal structures. Pathogenic variants in CLIC5 lead to autosomal recessive deafness and vestibular areflexia in humans. We are working towards restoring both auditory and vestibular functions in the Clic5 mutant mice. We created two synthetic AAV2/9-PHP.B vectors to evaluate therapeutic efficacy: self-complementary AAV (scAAV) and single-stranded AAV (ssAAV). Following their injection into the utricle of Clic5$^{c.680T>C}$ mice at P0, we assessed hearing through auditory brainstem response (ABR) and distortion product optoacoustic-emission (DPOAE) tests. Additionally, we examined vestibular function using open field, rotarod, and swimming tests. We observed improved hearing and vestibular function recovery and, in some cases, demonstrated ABR thresholds close to those of wild-type mice for each AAV vector. Implementing precision medicine, including gene therapy, in the field of hearing loss and translating it into the clinic will provide patients with improved medical management and rehabilitation.

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S7 L2 - The effects of epigenetic modifications on the efficacy of inner ear gene therapy

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Whirlin is necessary for hair cell stereocilia development. The *Whrn*$^{wi/wi}$ mouse does not express whirlin and exhibits abnormally short stereocilia bundles on cochlear and vestibular hair cells, leading to profound hearing loss and vestibular dysfunction. In a previous study, we showed that neonatal treatment with AAV8-whirlin was effective at lengthening the stereocilia bundles and partially restoring hearing and vestibular functions. However, when AAV8-whirlin was delivered to mature *Whrn*$^{wi/wi}$ ears (P30), the bundles remained abnormally short, despite the restoration of whirlin expression at the stereocilia tips. One possible explanation for this phenomenon is the difference in epigenetics between the neonatal and adult mouse inner ears.

In this study, we explore whether epigenetic modification using the histone deacetylase inhibitor SAHA can help to make the adult *Whrn*$^{wi/wi}$ ears more amenable to the effects of inner ear gene therapy. We find that the simultaneous application of SAHA with AAV8-whilrin increases stereocilia length in the *Whrn*$^{wi/wi}$ inner ears both *in vitro* and *in vivo*. Morphologically, hair cell stereocilia architecture is partially restored, and there is a reduction in the supernumerary rows of stereocilia in the transduced hair cells in *Whrn*$^{wi/wi}$ mice treated with AAV8-whirlin + SAHA. No improvement in the auditory function was observed, yet some adult *Whrn*$^{wi/wi}$ mice treated with AAV8-whirlin + SAHA exhibited partially restored vestibular function when compared to AAV8-whirlin alone, SAHA alone, and untreated *Whrn*$^{wi/wi}$ mice. Our results indicate that epigenetic modification can potentially be used to increase the efficacy of inner ear gene therapy in adult mammalian inner ears.

S7 L3 - Developing new AAV vectors for inner ear disorders: rational design and directed evolution

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Hearing loss (HL) affects approximately 20% of the global population and the treatments are currently limited to hearing aids and cochlear implants. Gene therapy offers the possibility to prevent or even cure HL. A significant limitation of current gene therapy approaches is the use of vectors that have been validated in neonatal animal models which do not reflect the transduction characteristics of adult tissue. To improve our delivery tool kit we have applied rational design and vector evolution strategies to produce a series of vectors targeted at specific inner ear cell types and vectors that can be delivered via transtympanic application in the adult cochlea.
Using phage panning to identify a series of peptides that bind inner ear tissue we created a series of vectors with the peptides inserted into the AAV2 coat. Structure-focused modeling of our novel vectors indicated a clear change in cell attachment receptor binding due to peptide insertion compared to its parental serotype AAV2. Predictions were confirmed using affinity chromatography and competition assays. After selecting vectors with optimized delivery to the spiral ganglion (Var9) we constructed a targeted vector that expressed the neurotrophic factor BDNF. Finally, in a neurotrophic gene therapy approach, Var9 effectively prevented SGN degeneration by overexpressing BDNF in SGN of deafened mice.
With the aim to optimize the adeno-associated virus (AAV) vector system for inner ear directed gene therapy, we generated AAV peptide display libraries based on the AAV1, AAV2 and AAV6 capsid backbones. All libraries present random unique 7-mer peptide inserts at variable region VIII of the capsid protein. We conducted high-throughput *in vivo* selection screens in the inner ear of adult mice, testing middle ear administration that allows vector entry into the inner ear without fenestration of the inner ear structures. Distinct variants were found to be accumulated to up to 5% for AAV2-based variants and up to 2.5% for AAV1-derived capsids after two rounds of *in vivo* selection. Three promising variants had the ability to transduce outer HCs, and many also targeted inner HCs. Almost half of the variants also strongly transduced all layers of the stria vascularis – a viable target tissue for the treatment of age-related HL – and the SGNs were targeted, with 4 variants being highly specific for SGNs.
Thus, we report on a set of promising new AAV variants targeted at specific cell types that can potentially be delivered by injection into the middle ear space thus forgoing round window injection.

S7 L4 - Human otic progenitor cell models of congenital hearing loss reveal potential pathophysiologic mechanisms of Zika virus and cytomegalovirus infections

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Congenital hearing loss is a common chronic condition affecting children in both developed and developing nations. Viruses correlated with congenital hearing loss include human cytomegalovirus (HCMV) and Zika virus (ZIKV), which causes congenital Zika syndrome. The mechanisms by which HCMV and ZIKV infections cause hearing loss are poorly understood. It is challenging to study human inner ear cells because they are encased in bone and also scarce as autopsy samples. Recent advances in culturing human stem cell-derived otic progenitor cells (OPCs) have allowed us herein to describe successful in vitro infection of OPCs with HCMV and ZIKV, and also to propose potential mechanisms by which each viral infection could affect hearing. We find that ZIKV infection rapidly and significantly induces the expression of type I interferon and interferon-stimulated genes, while OPC viability declines, at least in part, from apoptosis. In contrast, HCMV infection did not appear to upregulate interferons or cause a reduction in cell viability, and instead disrupted expression of key genes and pathways associated with inner ear development and function, including Cochlin, nerve growth factor receptor, SRY-box transcription factor 11, and transforming growth factor-beta signaling. These findings suggest that ZIKV and HCMV infections cause congenital hearing loss through distinct pathways, that is, by inducing progenitor cell death in the case of ZIKV infection, and by disruption of critical developmental pathways in the case of HCMV infection.

S7 L5 - Gene therapy in a rabbit model for USH3A

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Background: Autosomal recessive pathogenic variants in *CLRN1* (clarin 1) cause Usher syndrome type 3A (USH3A), characterized by slowly progressing hearing loss with post-lingual onset. In Ashkenazi Jews and Finns, USH3A represents up to 40% of USH cases. Animal models are needed to design therapies that reduce or prevent the inner ear pathologies associated with genetic deafness. In mouse models for USH3A, hearing loss is early onset and severe, and hair cells degenerate prior to cochlear maturation, reducing their utility as models for therapy. Here we describe a novel rabbit model for hearing loss in USH3A and attempts for therapies via AAV gene transfer using this model.
Methods: To generate the rabbit model, CRISPR/Cas9-mediated rabbit genome editing was used. To validate the model, ABRs were measured in anesthetized rabbits using TDT equipment. Tone bursts (15 ms) were delivered with 1 ms rise/fall times, presented 10 per second at 4, 12 and 16 kHz. Age-matched wild-type rabbits served as controls. For histology, bullae were removed and opened to expose cochleae. The stapes was removed and fresh 4% paraformaldehyde was perfused locally. For light microscopy sections, bullae were transferred into 5% EDTA with 0.25% glutaraldehyde added to soften the bone. Then cochleae were processed for JB-4 embedding followed by sectioning with a glass knife. For gene transfer experiments, AAV vectors with a GFP reporter gene insert, or AAV.Clrn1-Flag were injected into the perilymph. To assess reporter gene expression, bullae were lightly decalcified, dissected into organ of Corti segments, stained for GFP or FLAG, and for F-actin, and viewed in epi-fluorescence.
Results: ABR thresholds were elevated in 3-month-old CLRN1 rabbits compared to wild types, but the hearing loss was moderate. However, by 14 months of age, no hearing could be recorded at all tested frequencies. Histology showed that the severe hearing loss was accompanied by loss of cochlear hair cells. Injecting AAV.GFP into the perilymph of a wild-type ear resulted in transgene expression in sensory hair cells 14 days post-infusion. In a rabbit that received AAV.Clrn1-Flag at 5 weeks of age many surviving hair cells were Flag positive one month later, but thresholds did not improve. We are now extending the survival time to determine if viral mediated expression of CLRN1 can improve hearing thresholds compared to baseline.
Conclusions: The USH3A rabbit model we generated exhibits progressive loss of hearing over several months after birth, presenting a window for testing therapeutics including gene transfer approaches. Surgical injection of AAV vector into perilymph shows transfection of hair cells. Long term outcome of AAV.Clrn1 therapy is pending.
Support: National Institutes of Health grants R21 GM140359-01 (DY), 1R42EY035582-01 (DY), RO1 DC014832 (YR) and the The R. Jamison and Betty Williams Professorship (YR).

S7 L6 - Uncovering CHD7-SOX Gene Regulatory Networks to Advance the Diagnosis and Treatment of Genetic Hearing and Balance Disorders

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Hearing loss affects 1.5 billion people worldwide (~20% of the population). In newborn babies, roughly 1 in 500 are born with or develop hearing loss during childhood, and among these, up to 80% have a genetic basis. About 30% of genetic hearing loss is considered syndromic (associated with other clinical features) while the remaining 70% is nonsyndromic. There are currently 224 genes identified as being involved in nonsyndromic or syndromic genetic forms of hearing and balance disorders for which clinical testing is available. Many of these genes were initially discovered using standard linkage mapping techniques in families or, more recently, application of high throughput sequencing technologies. These exciting gene discoveries have also led to successes in development of gene-based therapeutics, as evidenced by the recent reports of OTOF-based gene therapies. Most forms of genetic deafness, however, remain inaccessible to gene or cell based therapies, and many individuals with suspected genetic deafness remain undiagnosed either due to limited access to diagnostics or lack of identified genetic causes. It is widely thought that at least some of the unsolved cases of genetic hearing loss are caused by genetic changes in the non-coding (and less understood) part of the human genome, epigenetic changes, digenic inheritance, modifier alleles, or complex gene-environment mechanisms. Our research has used mouse models to uncover gene regulatory networks that mediate early developmental events in the inner ear, with the goal of defining basic genetic mechanisms that control formation of vestibular and cochlear structures. I will share recent data showing that CHD7, an epigenetic regulator and ATP chromatin remodeler mutated in CHARGE syndrome (the most common monogenic cause of deaf-blindness), activates expression of the transcription factors SOX2 and SOX11 during mouse inner ear development. Together, these genes form genetic networks that are critical for proper cochlear and semicircular canal formation. When disrupted, cochlear hair cells and neurons, and vestibular apparati do not develop normally. Our results suggest that pathogenic changes in these genes could modify the functions of other genes in the network, thereby influencing both the diagnosis of and rational treatments for genetic hearing and balance disorders.

S8 L1 - Genetic Determinants of Hearing Loss and Cochlear Implant Outcomes in a Comprehensive German Cohort Study

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Background and objectives: Hereditary hearing loss is characterized by significant genetic and clinical heterogeneity, affecting diagnostic and therapeutic outcomes. This comprehensive study evaluates the genetic causes of hearing loss and the consequent variability in cochlear implant outcomes within a large, well-distributed German cohort, focusing on specific gene mutations and their impact on cochlear implant performance. To determine the genetic and clinical spectra of hereditary hearing loss and explore the relationship between genetic mutations, particularly those affecting neuronal components of the auditory pathway, and outcomes of cochlear implantation.

Methods: Over 500 families suspected of genetic hearing loss were subjected to targeted hearing loss gene sequencing. From this cohort, more than 100 cochlear implant (CI) recipients with a defined genetic etiology were analyzed for cochlear implant outcomes. Both studies focused on known syndromic and non-syndromic hearing loss genes, employing gene panel and whole genome sequencing. Postoperative CI outcomes were evaluated through extensive audiological follow-up, correlating genetic findings with postoperative performance levels.

Results: Genetic diagnostics identified causal variants in more than 35 genes from the hereditary hearing loss cohort, highlighting a predominant role of GJB2 and other genes like MYO15A, WFS1, SLC26A4, and COL11A1. Phenotypic characteristics such as early onset and higher grades of hearing loss were associated with better diagnostic yields. The distribution of causal genes in both cohorts pointed to autosomal-dominant genes playing a substantial role in late-onset hearing loss. In the CI cohort, postoperative outcomes across implanted ears revealed that pathogenic variants in sensory nonneural structures generally performed in upper quartiles, while mutations in genes expressed in the spiral ganglion demonstrated CI outcomes in the lower quartile range.

Conclusions: This analysis on hereditary hearing loss and cochlear implant outcomes underscores the complex relationship between genetic mutations and cochlear implant performance. The findings support the spiral ganglion hypothesis, suggesting that mutations affecting neuronal components of the cochlea can significantly impact CI outcomes. Targeted genetic testing not only provides a robust diagnostic yield but also aids in predicting cochlear implant efficacy, offering critical insights for managing hereditary hearing loss in clinical settings in particular in light of future gene therapy options.

S8 L2 - Lgr5+ endogenous progenitor cells in the human and mouse adult (deafened) cochlea

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Background: LGR5 positive supporting cells (SCs) in the cochlea give rise to hair cells (HCs) during embryonic development. Neonatal SCs have increased progenitor potential compared to adult and only a few studies (including ours) have shown survival of SCs with progenitor cell markers after severe HC loss in adult mice. In mammals, there is no evidence for spontaneous HC regeneration in adulthood. However, three-dimensional cultures have allowed the expansion and experimentation of human (and mouse) inner ear organoids. Here, we evaluated HC differentiation from human cochlear organoids and from adult normal-hearing and deafened mice.

Methods: Adult patients undergoing surgery for skull base tumors were included. Sensory epithelium of the cochlea and vestibular organ was collected in medium and tissue was digested to single cell suspension. Adult Lgr5-eGFP-IRES-creERT2 heterozygous mice were used. Mice were deafened with a single dose of furosemide in combination with kanamycin and deafening was confirmed by auditory brainstem responses (ABRs). Cochleas were harvested and digested to single cell suspension and after filtering, 3D drops were made with Matrigel. Cells were grown on expansion medium (EM) for 10 days and differentiation medium (DM) for 3-10 days after. Organoids were fixed, permeabilized and processed for immunofluorescence and whole-mounted for imaging in a confocal microscope.

Results: Vestibular-organ-derived organoids were generated in EM from all seven patients so far included. Cochlea-derived organoids were generated in five out of seven patients. After exposure to DM, vestibular organ-derived and cochlea-derived organoids produced MYO7A+ HC-like cells. Cochlear organoids from normal-hearing mice expressed LGR5 and Ki67 in EM and MYO7A after differentiation. Significantly less cochlear organoids were produced from deafened mice; however the organoids reached similar size as NH-cochlear organoids, expressed LGR5 and Ki67 in EM and MYO7A after differentiation.

Conclusions: Cochlear and vestibular tissue from adult patients (and adult normal-hearing and deafened mice) possess progenitor potential and the capacity to generate inner ear organoids *in vitro*. After differentiation, HCs were visible in tissue derived from human cochlea, human vestibular organ, and adult mouse cochlea. The adult inner ear has (limited) regenerative capacity and can produce new MYO7A+ HCs.

S8 L3 - Preclinical development of vesicle-enriched secretome fractions for the prevention of cochlear implantation trauma

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[*]*Cluster of Excellence Hearing4all*

Introduction:
After cochlear implantation, immune response can impair hearing performance or even lead to loss of residual hearing. So far, there are no approved pharmacological therapies available to treat hearing loss or to compensate for the immune response. Vesicle-enriched secretome fraction (VSF) derived from human umbilical cord mesenchymal stromal cells (UC-MSC) is a novel drug candidate intended to attenuate the reaction of the inner ear tissue in response to implantation trauma and related conditions. As a complex biological substance, VSF is a mixture of extracelluar vesicles (EV), particles and soluble factors exerting immunomodulatory or neuroprotective effects. Neuroprotection in dissociated rat spiral ganglion cell culture (in vitro) as well as attenuation of hearing threshold shifts and protection of hair cells in mice (in vivo) has been shown in previous studies. In preparation for a clinical trial, safety and biodistribution of VSF were investigated in mice after cochlear implantation trauma. In addition, preclinical investigation of safety aspects, biodistrubution within the cochlea and neuroprotective effects of VSF in combination with cochlear implantation trauma and associated conditions was performed in guinea pigs.

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S8 L4 - Efficacy of Small-Molecule Kv7.4 Agonist ACOU-085 in Protecting Against Cisplatin-Induced and Age-Related Hearing Loss

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Background: Hearing loss is exacerbated by aging, noise exposure, and chemotherapeutic agents like cisplatin. The Kv7.4, voltage-gated potassium channels expressed in the basal pole of outer hair cells (OHCs), is critical in mediating potassium efflux and maintaining the OHCs' resting potential. Impairment in these channels has been linked to ototoxic, age-, and noise-related hearing loss. The therapeutic potential of ACOU-085, a novel small-molecule Kv7.4 agonist, is investigated in mitigating hearing loss due to aging and cisplatin exposure in experimental models.

Methods: Two distinct animal models were employed to assess the efficacy of ACOU-085. In the first model, senescence-accelerated mouse prone 8 (SAMP8), ACOU-085 was administered via transtympanic injection. In the guinea pig model, cisplatin was locally applied to the round window, followed by local administration of ACOU-085 using an osmotic minipump. Auditory function was evaluated using auditory brainstem response (ABR) and compound action potential (CAP) responses, with cochleae extracted for histologic cytocochleogram analysis to quantify OHC loss.

Results: In the SAMP8 mouse model, ACOU-085 demonstrated a dose-dependent preservation of hearing, significantly reducing age-related ABR threshold shifts and OHC loss, particularly in the high-frequency range. In the guinea pig model, ACOU-085 significantly mitigated cisplatin-induced functional hearing loss and protected both inner and outer hair cells across multiple dosages, with the most substantial protection observed at higher concentrations.

Conclusion: ACOU-085 exhibits potent otoprotective effects in multiple preclinical models, offering promising prospects for treating various forms of hearing loss. These findings support the ongoing clinical development of ACOU-085, including an ongoing Phase 2 trial aimed at evaluating otoprotection in cisplatin-treated cancer patients. The efficacy of this agonist against both age-related and ototoxic-induced hearing loss underscores its potential as a versatile therapeutic agent for hearing loss.

Conflict of interest:
Hubert Löwenheim is scientific founder, shareholder, and board member of Acousia Therapeutics GmbH Tübingen

S8 L5 - Regulatory network of mTORC2 in an auditory hair cells line

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Background:
The mammalian Target of Rapamycin (mTOR) kinase is part of a signaling network regulating fundamental cellular processes such as growth, metabolism and aging. It is found in two structurally and functionally distinct multiprotein complexes, mTOR complex 1 (mTORC1) and mTORC2, each of which signals via its own signaling pathway. We recently reported on stunted and absent stereocilia and a reduced synapse number in inner ear hair cells in mice lacking a functional mTORC2 complex in auditory hair cells. Little is still known on the molecular basis of these findings.

Material and Methods:
To further elucidate the role of mTORC2 in inner ear cells, we generated a Rictor knockout cell line from HEI-OC1 auditory cells. We then performed morphological analysis of these cells and used a proteomic approach to define the proteomic network.

Results:
mTORC2 deficient auditory cells exhibited decreased proliferation rates and significant alterations in actin cytoskeleton morphology. Additionally, we observed reduction in the phosphorylation of protein kinase C alpha (PKCα) and disrupted actin polymerization in mTORC2 deficient cells. Proteomic analysis revealed substantial modifications in actin cytoskeletal processes, characterized by numerous up- and downregulated proteins.

Discussion and Conclusion:
The mTORC2 signaling pathway plays an important role in regulating auditory hair cell structure and function via regulation of the actin cytoskeleton. These results provide molecular insights on a central regulator of cochlear hair cells and thus hearing.

S9 L1 - Tumor tissue hnRNP M as a potential biomarker of disease-specific mortality in patients with early-stage cutaneous head and neck melanoma: A proteomics-based study

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Background:
Breslow tumor thickness and mitotic rate are standardly used for risk stratification of patients with malignant melanoma. However, their prognostic value is relatively limited and a need for improved prognostication has been advocated. We aimed to screen the tumor tissue proteome in a search for potentially useful prognostic factors in early-stage cutaneous head and neck melanoma.

Methodology and Findings:
Proteomic profiles of archival formalin-fixed tissue samples of 31 patients (age 23-90 years) with early-stage head and neck cutaneous malignant melanoma (American Joint Committee on Cancer, AJCC, stage I/II) were determined and expression intensities were compared to those of melanocytic nevi, yielding ratios used in data analysis. Medical charts were retrospectively reviewed to determine time elapsed since diagnosis to disease-specific death or censoring. In a multivariate recursive partitioning analysis (as per AJCC guidelines), higher expression levels of heterogeneous nuclear ribonucleoprotein M (hnRNP M) [n = 18, HR = 1.94 vs. the entire cohort; HR = 5.95 (95%CI 2.43-14.5) for "high" vs. "low" (n = 13)] and of heat shock protein 90 alpha (HSP 90α) [n = 17, HR = 2.09 vs. the entire cohort; HR = 4.59 (95%CI 1.87-11.2) for "high" vs. "low" (n = 14)] were each independently strongly associated with higher mortality (accounting for clinical and standard pathohistological features). Higher Breslow thickness and mitotic rate were associated with higher mortality only when proteomic data were disregarded.

Conclusions and Significance:
Data suggest that tumor tissue expression of hnRNP M deserves further investigation and clinical validation as potential novel risk stratification aids in patients with stage I-II cutaneous head and neck malignant melanoma.

S9 L2 - Application of artificial intelligence in endoscopic diagnosis of glottic lesions

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Background: We have been using upper gastrointestinal endoscopy (upper GI endoscopy) for the early diagnosis, transoral surgery, and post-treatment follow-up of laryngopharyngeal cancer due to the usefulness of its high-resolution images, magnified observation, and image-enhancement functions. In this study, we developed an endoscopic artificial intelligence (AI)-based endoscopic diagnostic support system for laryngopharyngeal cancer and, this time, verified its usefulness in glottic cancer, considering that improving the diagnostic ability for early laryngopharyngeal cancer is an essential issue in cancer screening using upper GI endoscopy.
Materials and Methods: First, we prepared training data by positioning the circumscribed rectangle of the lesion in endoscopic images of 120 glottic cancer cases taken by upper GI endoscopy from 2015 to 2021, labeling distant images as "tumor" and close-up images as "glottic cancer." Deep learning was performed using the multilayer neural network YOLOv5. A white light endoscopy (WLE) model and a narrow band imaging (NBI) model were created using 845 training image data, respectively, and cross-validation was performed. Diagnostic accuracy was evaluated using the accuracy rate, sensitivity, specificity, and positive predictive value.
Second, only NBI images of 179 cases of glottic tumors, including glottic cancer, leukoplakia, granuloma, and vocal cord polyps, were used as training data, and deep learning was performed after labeling in the same manner as above. The training data consisted of 1,750 images, with the breakdown of labels being 529 "tumor," 880 "glottic cancer," 130 "leukoplakia," 85 "granuloma," and 126 "vocal cord polyp." For validation, generalization performance was evaluated using 234 still images not used in the training data (58 "tumor," 102 "glottic cancer," 11 "leukoplakia," 11 "granuloma," 12 "vocal cord polyp," and 40 "normal larynx").
Results: The accuracy rate of the WLE/NBI model was 82.7/84.8%, the sensitivity was 82.5/87.9%, the specificity was 89.7/92.0%, and the positive predictive value was 84.7/86.9%, showing that the NBI model had a higher diagnostic accuracy than the WLE model. The accuracy rate of the NBI model for tumors/glottic cancer/leukoplakia/granulomas/vocal cord polyps was 94/95.7/99.6/98.7/99.1%, the sensitivity was 98.3/91.2/100.0/72.7/83.3%, the specificity was 92.6/99.2/99.6/100/100%, and the positive predictive value was 81.4/98.9/91.7/100/100%.
Conclusion: These results suggest that AI-based endoscopic diagnostic support systems are helpful for endoscopic screening of glottic lesions.

S9 L3 – Intraoperative nerve-specific fluorescence imaging: first in-human results

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Background:
Iatrogenic nerve injury is a frequent complication during routine surgical procedures and is associated with significant and often permanent morbidity. Such injuries are negatively correlated with surgeon experience, visualization, and anatomic consistency. To address this critical unmet clinical need, we evaluated a first-in-class nerve-specific fluorescent imaging agent to improve detection of nerves.

Methods:
We assessed a novel fluorescein labeled peptide (bevonescein) that selectively binds to nerve tissue (NCT04420689). We completed a prospective, dose ranging, open-label, multi-center phase 1-2 trial to evaluate the safety, pharmacokinetics, and efficacy of bevonescein in adults undergoing thyroidectomy, parotidectomy, cervical lymphadenectomy (NCT04420689). The agent was assessed for safety and signal-to-background ratio (SBR) at a range of doses (100, 200, 400, 500, 600 mg) and in early (1-3 hours) and late (3-5 hours) timing cohorts.

Results:
Twenty-seven participants were infused with the agent without a dose limiting toxicity. The serum half-life was 30 minutes. The optimal imaging dose by objective measures was identified at 500 mg with the fluorescence SBR (2.1±0.8) significantly higher than that of white light (1.3±0.2; $p=0.003$). At this dose, the 4-point discrete Likert scale scoring by the surgical team demonstrated improved nerve identification using fluorescence (3.3) compared to white light (2.6, $p<0.001$) and moderate improvement in identification nerve branch points (2.1 compared to 1.9, $p<0.005$).

Conclusions:
This is the first clinical study to demonstrate the value of a systemically injected nerve-specific agent. A preoperative intravenous infusion of bevonescein was safe and produced clinically meaningful intraoperative nerve visualization compared to standard of care.

S9 L4 - Ultrasound guided procedures in the Head and Neck: A clinician centered model

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Background: Cytological evaluation of samples obtained by fine needle aspiration (FNA) is a well-established and reliable tool with a very low morbidity and risk of tumor seeding. The cost-effectiveness and diagnostic accuracy is increased by ultrasound (US) guidance and by the presence of a cytologist to make a rapid on-site evaluation (ROSE) of the sample, allowing to assess immediately the need for a further sampling of the lesions. In selected cases the same US guidance can be exploited for core/gross needle biopsies, which allows obtaining samples for histology and potentially for immunohistochemistry.
The anatomy of head and neck, being the only real barriers the bulky bony structures, such as the mandible and splanchnocranium, allows the US sampling of almost every lesion, especially with the valid support of US guidance.
The definition of either benign or malignant nature of the lesions remains the first priority and the main scope of these assays, both in the follow up or staging of known primary lesion and in diagnosing the natuter of head and neck masses without an obvious origin from mucous and/or cutaneous surfaces.
Aim of the study is to evaluate the utility of a lump clinic involving clinicians and pathologists and integrating US guided procedures, clinical assessment and multidisciplinary discussion in the diagnostic approach to head and neck deep masses.
Methods: We conducted an analysis of a monoinstitutional database encompassing all patients who underwent US guided sampling for head and neck lesions at the Lump Clinic within the Otolaryngology Division of the University Hospital of Sassari, Italy, between 2017 and 2024. After obtaining a formal cytological report, all cases underwent a comprehensive evaluation by the otolaryngologist and histopathologist, combining the cytological findings with clinical history, physical examination, ultrasonographic features, and a multiparametric diagnosis could be formulated in many of the non-diagnostic samples. In the population who subsequently underwent surgery, sensitivity and specificity of US guided cytology, and possibly histology, and of multiparametric analysis have been assessed according to their ability to predict the final histology and the malignancy of the lesion.
Results: A total of 810 US guided procedures were performed on major salivary gland lesions in the present database. In 51.8% surgery was subsequently performed and a definitive histological report was available. Sensitivity in predicting malignancy was 97.7%. The multiparametric diagnosis was formulated in 80% of non-diagnostic/inadequate samples at cytology, drastically reducing the inadequacy especially in case of Warthintumor.

Discussion: The present work fully confirms the utility and reliability of US guided procedures and of a multidisciplinary lump clinic in the management of neck masses. We do believe that the present results are presumably fully replicable provided that the procedure is performed in a multidisciplinary context involving the surgeon and histopathologist, under ultrasound guidance and with the possibility to repeat sampling cytological sampling or switch to a core/gross needle biopsy if required according to the rapid on site evaluation. This also outlines the added value of ultrasonography in the hands of the head and neck surgeon who should systematically associate it to collection of clinical history, endoscopy and physical examination in its initial approach to neck masses.

***S9 L5* - 3D-image-guided navigation with touchless gesture user interface during minimally invasive head and neck surgery: do we have "biomechanics" of the new era in our personalized contactless hand-gesture non-invasive surgeon-computer interaction?**

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In modern operation rooms, with the innovative application of medical informatics, it is possible to enable many aspects of surgeries that were not able to be addressed before. Definitely, one of these is contactless surgery (CS), with planning and controlling the visualization of medical data. We started our initial research by applying virtual reality (VR) concepts in our first Tele-3D-CAS in rhinology (1998), where we implemented a new framework for the transfer of computer data (images, 3D models) in real-time during the surgery and, in parallel, of the encoded live video signals. We demonstrated this approach with an example of our 3D-computer assisted navigation rinosurgery (1994) with simulation and planning of the course of an endoscopic operation per virtual endoscopy/surgery (VE/VS), which overcomes difficulties of conventional endoscopies, such as “standard” FESS or Tele-FESS.
In our CS-concept (from 2017-2024), based on our latest EU-research “EU-EIT Health RIS Innovation 2020 Grant”, we were focused: a) on improving the “In the Air” human–computer interaction during surgery in the clinical environment, b) set the problem of navigation through the human body, c) our input modalities for surgeon–computer interaction and motion recognition methods used for controlling the contactless 3D-VE, d) completely new framework for hand and motion detection based on augmented reality (AR), e) we developed a contactless interface for a surgeon to control the visualization options in our DICOM-viewer platform, that uses a stereo camera as a sensor device input that controls hand/finger motions in contactless mode, and applied it to 3D-VE and 3D-VS, f) our proposal for defining motion parameters in contactless, incisionless surgeries, g) we implemented motion tracking using stereo cameras with depth resolution and precise shutter sensors for depth streaming, h) our CS-provides contactless control with a range up to 2–3 m that definitely enables the application in the OR. In modern medical world, the surgeon, thinks differently, with a new visualization aspect and understanding of the ecosystem, visualization space, and self-and anatomy-awareness of his patients. Our newest CS-approach could be an important step towards the strategy of enhancing surgeons’ capacities and increasing their satisfaction and precision since we enable the integration of real and virtual objects in the surgical field, which enables better surgeon’s experience, more precise surgery, real-time feedback, depth motion tracking, and contactless control of visualization, which gives freedom during the surgery. However, does our CS really represent the future of smart surgery? Do we really have real technological advances in ENT-surgery in our hands, as the great Professor Heinz Stammberger once said?

S9 L6 - Usefulness of ultra high-resolution computed tomography for preoperative staging of the tongue cancer

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Background: Computed tomography (CT), Magnetic Resonance Imaging (MRI), ultrasonography (US), and positron emission tomography are standard modalities for the clinical staging of head and neck cancer. Especially, CT is a conventional method that can acquire three-dimensional information in a short time and is widely used for evaluation.
In the 8th edition of the American Joint Committee on Cancer/TNM classification, the depth of invasion (DOI) was added to the T classification of tongue cancer in addition to tumor size, requiring more accurate preoperative evaluation. However, CT imaging of the oral region has the problem of generating metallic artifacts due to dental metal. Depending on the type of dental metal, the artifact can cause image distortion and CT value reduction over a wide area, from the tongue and gingiva to the oropharynx and parotid gland, making it difficult to evaluate the lesion precisely.
Ultra high-resolution CT (UHR CT), Aquilion Precision (Canon Medical Systems co.), is capable of resolving anatomy as small as 150 microns with an all-new detector as well as tube, gantry and reconstruction technologies. Combining Single Energy Metal Artifact Reduction (SEMAR) and UHR CT enables precise visualization of lesions, even in cases with dental metal appliances. In addition, the imaging efficiency can be improved by modifying a patient's position at the time of imaging. In this retrospective study, we examined the usefulness of these techniques for the clinical staging of tongue cancer.
Subjects and Methods: Twenty-one consecutive patients with tongue cancer who underwent this imaging method in preoperative clinical staging were included in this study. CT examination was done with UHR CT. At the examination, gauze was placed around the patient's tongue and the image was taken with the mouth open to reduce artifact. The visualization rate of the primary site was compared between the conventional method and this imaging method. DOI of tongue cancer was measured by CT, MRI, and ultrasound, and errors between pathologic and imaging DOI were statistically analyzed.
Results: Eighteen of 21 patients had dental metal. Conventional method did not visualize the primary lesion in all patients with dental metal, whereas this imaging method visualized the lesion in 15 of 18 patients (83%). Spearman's rank correlation coefficient showed a correlation with pathologic DOI for all imaging modalities. DOI of CT, MRI, and US were greater than pathologic DOI, with errors of 1.6 mm, 1.5 mm, and 1.2 mm, respectively.
Conclusions: Ultra high-resolution CT is suggested to be useful in the preoperative diagnosis of tongue cancer.

S10 L1 - Extracapsular dissection in benign parotid gland tumors: single institution experience

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A retrospective evaluation of the records of all patients treated for benign parotid tumors at a tertiary referral center between 2000 and 2022 was carried out. Surgical methods were classified into four groups: extracapsular dissection, partial superficial parotidectomy, superficial parotidectomy and complete parotidectomy.
A total of 4037 patients were included in the study. Our analysis demonstrated an increase in the total number of parotidectomies for benign lesions from 71 (2000) to 298 (2022) per year, mostly due to the increase in extracapsular dissection (from 9 to 212). The increased performance of less radical surgery was associated with a significantly decreased incidence of perioperative complications.

Conclusion:
Our study showed that the increased performance of less radical surgery was associated with better functional outcomes over the years

S10 L2 - Modern Thyroid Surgery and Parathyroid gland Vasculature preservation during total Thyroidectomy

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Objectives: To go over the past and future in regards to thyroid surgery
To go over all the recent advances in in thyroid surgery and to evaluate the effect of preserving the parathyroid gland vasculature on the rate of postoperative transient hypoparathyroidism and hypocalcemia and the different modern methods in that regard.
To go over the new technologies in protecting the recurrent laryngeal nerve during thyroid surgery.
to go over the recent results in our institution using the new methods of preserving parathyroid gland and nerve monitoring in protecting the recurrent laryngeal nerve
Then I will go over our most recent study that will talk about Parathyroid gland Vasculature preservation during total Thyroidectomy: Risk of post operative hypoparathyroidism

Background: Hypoparathyroidism is among the most common complications soon after total thyroidectomy and it can place a major strain on both the patient and the surgeon. There is little current research supporting either method of total thyroidectomy (Traditional vs. parathyroid gland vasculature preservation). Our aim is to evaluate the effect of preserving the parathyroid gland vasculature against not preserving them on the rate of postoperative transient hypoparathyroidism.

Methods: Patients who underwent total thyroidectomy using the traditional method (Group 1, Sep 2021 to May 2022) and the method that preserved the parathyroid gland vasculature (Group 2, June 2022 to December 2022) were compared. These patients' parathyroid hormone levels were measured postoperatively, to analyze the incidence of hypoparathyroidism in both groups.

Result: Total thyroidectomy was performed on 65 individuals with thyroid disorders, including 33 patients in group 1 (9 males and 24 females) with a mean age of 42 ± 11.53 years and 32 patients (11 males and 21 females) in group 2 with a mean age of 45 ± 12.26 years. The incidence of transient hypoparathyroidism at postoperative day 1 in group 1 was significantly higher than in group 2, 39.4% and 15.6% respectively ($p < 0.03$). None of the patients in both groups suffered from permanent hypoparathyroidism.

Conclusion: Parathyroid gland vasculature preservation in-situ technique was remarked, as it showed there is a significant association with higher PTH level and lower incidence of transient hypoparathyroidism after total thyroidectomy.

S10 L3 - Endoscopic laryngopharyngeal surgery for early stage hypopharyngeal cancers

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Background: Hypopharyngeal cancer (HPC) accounts for approximately 10% of all head and neck squamous cell carcinomas. Previously, most HPC cases tended to present at an advanced stage and required multimodal treatments. However, the prognosis of HPC was not satisfactory because most cases developed regional lymph node metastases or distant metastases during the clinical course.
Recent innovations in optical technology have enabled the detection of HPC at very early stages. With the increased number of early stage HPC cases, the premise of transoral surgery for early stage HPCs has wide global acceptance. However, transoral resections of HPC are not always easy due to the technical difficulties in obtaining adequate exposure of the hypopharynx.
Endoscopic laryngopharyngeal surgery (ELPS) is one of the transoral surgical techniques used for pharyngeal and laryngeal lesions. It was developed from endoscopic submucosal dissection techniques for gastric and esophageal cancer in early 2000s. The main benefit of this procedure is the excellent visualization of the hypopharynx with the aid of a curved laryngo-pharyngoscope. Since 2010, we have treated early stage HPCs with ELPS, and herein report the outcomes of this transoral procedure.

Materials and Methods: One hundred and eight patients with early stage HPCs were treated by ELPS from February 2010 to February 2017, and the clinical courses of the patients were reviewed.

Results: Four females and 104 males (average: 65.8 yo) were included in this study. Some patients had multiple lesions and a total of 119 HPCs (Tis: 47, T1: 43, T2: 20, T3: 9) were treated with ELPS. Five patients presented with nodal metastases. In all cases, the hypopharynx was well visualized with sufficient working space, and no cases required a change in surgical approach. All post-operative complications were safely managed. In regard to the oncological outcomes, the 3-year and 5-year overall survival rate was 93.6% and 85.5%, respectively.

Conclusions: During ELPS, the hypopharynx was well visualized providing sufficient working space for the resection. The procedure was safe and feasible for HPCs and exhibited very good oncological outcomes. ELPS is thought to be a very effective surgical alternative for early stage HPCs.

S10 L4 - Reconstruction of a tracheal defect using a 3D printed leaf-stacked scaffold implanted with mesenchymal stem cell spheroids

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Objectives:
The mesenchymal stem cell (MSC) stimulates angiogenesis and anti-inflammatory responses, and stem cell spheroid has been shown to can enhance these features. Cell attachment to tracheal scaffolds composed of polycaprolactone is problematic because of their hydrophobic nature, and surface modification is known to promote cell attachment. The goal of this research was to assess our innovative 3D-printed leaf-stacked scaffold and MSC spheroid in tracheal regeneration.

Methods:
In vitro study was performed on various scaffold to test cell attachment. The rabbits were divided into four groups based on the type of MSC implantation at the 3D-printed leaf-stacked scaffolds: no MSC implanted (no MSC group), monolayer MSC implanted at the inner surface (inner MSC group), MSC spheroid implanted at the outer surface (outer MSC spheroid group), and both inner monolayer MSC and outer MSC spheroid (both MSC group). Tracheal defects were created, and reconstruction was performed using tracheal scaffold. 14 weeks later, the tracheas were harvested for structural and histological analysis.

Results:
The leaf-stacked polycaprolactone membrane exhibited the best attachment of implanted MSC compared to tissue culture polystyrene and polycaprolactone film . All subjects survived for 14 weeks. A higher number of mature vessels and larger M2/M1 ratios were observed in the outer MSC spheroid group and the both MSC group than the other groups. The inner single MSC group and both MSC group exhibited better mucosal regeneration than the other groups, while the no MSC group showed the poorest mucosal regeneration.

Conclusion:
MSC spheroid implanted on leaf-stacked scaffold exhibited good neo-angiogenesis, mucosal regeneration, and an anti-inflammatory status, demonstrating the potential for promising tracheal regeneration.

S10 L5 - Carotid Body Tumors: Association between SDHB Immunohistochemistry Results and Genetic Testing

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Background:
Carotid body tumors (CBT) are rare tumors that occur at the bifurcation of the carotid artery and are pathologically classified as paragangliomas. It has been revealed that germline genetic abnormalities are involved in the development of these tumors, particularly mutations in the genes for the subunits of succinate dehydrogenase (SDH). The effectiveness of immunohistochemical staining for SDHB protein in tumor tissues has been reported to infer these genetic abnormalities.

Subjects and Methods:
Among 54 patients who visited our hospital between 2011 and 2023 and underwent genetic analysis using blood-derived DNA, 30 underwent surgical resection. Immunohistochemical staining was performed on the surgical specimens to evaluate SDHB protein expression.

Results:
The patient's ages ranged from 28 to 63 years, with a median age of 44. There were 10 males and 20 females. According to the Shamblin classification, which indicates tumor progression, there were 17 cases of Class I, 9 of Class II, and 4 of Class III. Fourteen of the 30 cases had germline genetic variants in SDHx (including variants of unknown significance, VUS). In 16 cases, whole exome sequencing was conducted, and no abnormalities in genes related to paraganglioma development, including SDHx, were found.

In the 14 cases with genetic variants in SDHx, 13 showed negative SDHB immunostaining, and one was positive. This positive case had a VUS in SDHB. On the other hand, among the 16 cases without genetic variants in SDHx, 12 showed negative SDHB immunostaining, and four were positive.

Discussion:
The expression of SDHB in tumor tissues has been shown to predict abnormalities in SDHx genes. Additionally, there are cases (40% of the total) where no genetic abnormalities in SDHx are found, yet SDHB immunostaining is negative. In these cases, a mechanism that suppresses the expression of SDHx within the tumor may be presumed.

S10 L6 - Long-term survival in pediatric tracheostomy with different socioeconomic status: A population-based study

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Introduction:
This study aims to clarify the impact of socioeconomic status on long-term outcomes of pediatric tracheostomy in Taiwan.

Material and Methods:
All inpatients < 18 years who received tracheostomy between 2000 and 2014 were identified from the Taiwan's National Health Insurance Research Database, and followed up with them until 2019. Socioeconomic status was determined by the monthly income of their caregivers at the year of tracheostomy and classified into low- middle- and high-income. Outcome variables include in-hospital death, hospital stay, readmission, 1-year, 5-year, and overall mortality.

Results:
Overall, 2031 children were identified (mean age, 8.8 years; 64% boys), in which 707 children were low-income group, 615 children were middle-income group, and 709 children were high-income group. The median monthly income was $32.5, $710.4, and $1123.8 for low-, middle-, and high-income group, respectively. Children in low-income group had a significantly higher rate of in-hospital death (24.2% vs. 5.1%), 1-year mortality (42.2% vs. 9.6%), 5-year mortality (68.0% vs. 19.6%), and overall mortality (77.5% vs. 29.8%) compared to those in high-income group (all $P < 0.001$). Multivariable model revealed children in low-income group significantly increased the risk of in-hospital death (hazard ratio [HR] = 6.38), 1-year mortality (HR = 5.28), 5-year mortality (HR = 4.99), and overall mortality (HR = 4.48) than those in high-income group. Hospital stay and readmission rate was slightly higher in low-income group but did not reach statistical significance.

Conclusions:
Lower socioeconomic status was associated with increased risk of mortality in Taiwanese children with tracheostomy.

S11 L1 - The Development of a Newly Invented Inner Ear Implant Device (HIBIKI): Results of animal experiment

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Over the past 30 years, cochlear implant (CI) has been developed mechanically and biotechnologically.
We are now developing new CI device. Newly invented device is called artificial auditory epithelium (AAE) or HIBIKI device. The mechanism of HIBIKI device is to vibrate the basilar membrane of the cochlea and cause distortions of the vibrating portion of HIBIKI device. Then electricity produced by the vibrating portion is lead to the spiral ganglion (cochlear nerve) by electrodes and stimulate it. The characteristic of this device is totally-implantable in the inner ear, as well as there is no need of extra battery.
A prototype of HIBIKI device has been already made. It can imitate the functions of sensory epithelia of the cochlea and transform vibratory movements into electric signals with frequency characteristics. It is fabricated to verify the validity of the basic mechanisms and has gradient in its width which is also the characteristic of the basilar membrane of the cochlea.
We have also invented totally implanted HIBIKI device for animal use.
This HIBIKI device can generate electrical potentials in response to sound stimuli that are able to induce auditory brain stem responses in deafened guinea pigs.
Together with the mechanism of HIBIKI device the results of all animal experiments using HIBIKI device will be presented.

S11 L2 - Investigation of Local Dexamethasone Delivery Techniques to the Inner Ear in a Large Animal Model

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Background: Efficient compound delivery to the inner ear remains a significant hurdle to be overcome. As systemic drug delivery to the cochlea usually requires high dosages to overcome the blood-labyrinth-barrier often associated with considerable side effects, local drug delivery presents a suitable and effective alternative for inner ear drug delivery. Nevertheless, local drug delivery methods can suffer from diffusion and distribution problems into or within the cochlea and few is known about the in-vivo distribution of active compounds after local application to an inner ear of human-like size. Hence, our goal was to investigate the intracochlear (IC) distribution of the steroid dexamethasone (DEX) after local administration using different delivery methods in a large animal model.

Methods: We applied DEX in piglets via intratympanic (IT) or IC delivery routes. For IT delivery, DEX was injected through the tympanic membrane formulated as either a fluid or a thermoreversible hydrogel. For IC delivery, either fluid DEX solution was injected into the cochlea using a catheter system or a custom-made 10%-DEX-PLGA implant was inserted into the cochlea. The distribution of DEX was subsequently determined via apical perilymph sampling using high-performance liquid chromatography at predefined time points after application.

Results: Using the catheter for direct IC drug delivery achieved the overall highest DEX concentrations and an even distribution across the cochlea. IT delivery of hydrogel-bound DEX resulted in higher drug concentrations compared to the DEX-fluid delivery. Latter additionally displayed a significant drop in drug concentrations towards the cochlear apex. Finally, even though the total DEX-concentration after PLGA implantation was lowest across all groups, sustained drug delivery up to seven days after PLGA insertion was achievable.

Discussion: This work is the first to investigate and compare different local drug delivery techniques to the cochlea of a large animal model. We show that different delivery methods result in distinct drug distribution profiles with varying concentration peaks. Due to the high translatability of this model, we suggest that different delivery techniques may be suitable for diverse inner ear diseases, which should be considered in the clinical decision-making process.

S11 L3 - Does Cochlear Implant Electrode Array Design Affect Audiologic Outcomes? A Systematic Review and Meta-Analysis

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Objective:
There is conflicting literature regarding whether electrode array (EA) selection impacts audiologic outcomes for patients with cochlear implants (CI). We sought to compare outcomes for the two EA designs, precurved and straight.
Databases Reviewed: PubMed, Scopus, and CINAHL.

Methods:
Following PRISMA guidelines, systematic review and meta-analysis were performed. Included studies reported speech recognition scores or hearing preservation (HP) rates for patients with postlingual hearing loss who underwent CI with either EA type. Meta-analyses of mean difference and proportions were conducted. Speech score changes were reported as difference in percentage points from baseline.

Results:
Of 3,748 unique abstracts screened, 77 studies were included, comprising 3,949 patients (n=4,196 ears). Mean improvement of word recognition scores for patients with precurved EAs (47.1 percentage points above baseline; 95%CI, 43.0-51.2%) was significantly superior to that of patients with straight EAs (35.5%; 95%CI, 28.9-42.1%); p=0.004. There was no significant difference between mean improvement of sentence in quiet scores for patients with precurved EAs (51.8%; 95%CI, 42.9-60.7%) and those with straight EAs (52.6%; 95%CI, 44.7-60.4%); p=0.90. No statistically difference was found between mean improvement of sentences in noise for patients with precurved EAs (32.6%; 95%CI, 26.2-39.0%) and those with straight EAs (33.9%; 95%CI, 20.9-46.9%); p=0.87. There were no statistically significant differences in HP or pure-tone averages between EA types.

Conclusion:
Patients who received precurved EAs experienced greater improvement in mean word scores compared to those with straight EAs. There was no superior EA design regarding sentence recognition or hearing preservation.

S11 L4 - FLEX 34 – cochlear implant electrode: first experience and results

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Introduction: According to recent scientific publications there is a correlation in outcome-performance of cochlear implantation and electrode lenght, concerning the anatomical coverage of the full length of scala tympany. Individual selection of Cochlear Implant electrode array length is directly related to outcome in speech perception and listening skills, especially in difficult listening situations. Our aim was to present the first results with the new Flex 34 Cochlear Implant array (intracochlear length 34mm) in individual patients with an anatomical cochlear duct length of more than 34 mm.
Methods: In a retrospective study we analyzed the data of adult Flex 34 electrode cochlear implant recipients. In preop evaluation we collected duration of deafness, aethiology of defaness, pure tone audiometry and listening skills. As well as postop hearing performance with Flex 34 Cochlear implant, one, three and six month post implant activation.
Results: We implanted 12 adult patients (so far no pediatric patient was identified with a cochlear duct lenght longer 34mm). Cochlear duct lenght was measured through CT and MRI scans and Otoplan® software. Cochlear duct lenght in our patiens was in mean 36mm long. There were no intra- or post operative negative side effects or complications in all surgeries. All 12 adult patients had a full insertion of the Flex 34 cochlear implant array. Listening skills and hearing performance were in so far known good levels. In Vienna one out of 10 adult cochlear implant candidates was eligable for a Flex 34 electrode array. In Wels – Griesskirchen, one out of six candidates. This might reflect the differences in skull and cochlear anatomy in between the Vienna and the State of Upper Austria population. As a side result from our investigations the so called dogma that the cochea is already fully anatomically grown up at birth might be questionable, as we see significant differences in cochlear duct lenght in babies younger 12 months old compared to adults.
Conclusion: Using Otoplan® Software to measure cochlear duct lenght prior cochlear implantation is a requirement to use the Flex 34 cochlear impant electrode array. In selected candidates with proper anatomy, the Flex 34 CI is a safe and effective treatment and in our opinion better then a shorter electrode array in a long scala tympany. The pure anatomical size compared in between babies younger then 12 month old and fully grown up adults need to be further investigated in more patients.

S11 L5 - X-ray Guided Anatomy-Based Fitting

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Background:
Anatomy-based fitting (ABF) is a new research area in the field of cochlear implants (CIs). Despite the reported benefits and acceptable levels of ABF among CI recipients, some limitations remain, like the postoperative computed tomography (CT) scan, which is preferred for confirming electrode array insertion.

Objective:
This study aimed to investigate the feasibility of using plain film radiography (X-ray) for postoperative electrode detection and for building ABF as an alternative to CT.

Methods:
A total of 53 ears with CI were studied. All cases had routine post-insertion X-rays in the cochlear view and additionally underwent postoperative CT. The insertion angles and center frequencies measured by two independent observers were compared for each imaging modality. The angular insertion depth and center frequencies resulting from the X-ray and CT scans were then compared.

Results:
No significant differences were observed between the X-ray- and CT-measured angles for the electrode contacts. Radiographic measurements between the two readers showed an almost perfect (≥0.8) or substantial (0.71) intraclass correlation coefficient along the electrode contacts. X-ray images showed a mean difference of 4.7 degrees from CT. The mean semitone deviation of the central frequency between the CT and X-ray images was 0.6.

Conclusions:
X-ray imaging provides a valid and easy-to-perform alternative to CT imaging, with less radiation exposure and lower costs. The radiographs showed excellent concordance with the CT-measured angular insertion depth and consequently with the central frequency for most electrode contacts. Therefore, plain X-ray could be a viable alternative in building ABF for the CI recipients.

S11 L6 - The application of the exoscope in Otorhinolaryngology: Case Cochlear Implantation

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Background:
Digital high-definition three-dimensional (3D) exoscope systems have evolved to become a viable alternative to the operating microscope (OM) for surgeries in Otorhinolaryngology. We investigated the feasibility of a footswitch operated robotic arm digital 3D exoscope system in the highly challenging setting of cochlear implantation and compare it to the OM.

Material and Methods:
Cochlear implantation was performed with the exoscope on unselected patients with normal temporal anatomy. The control group that underwent cochlear implantation with the OM were case matched with respect to age, anatomy, surgical technique and type of anesthesia.

Results:
11 patients (13 ears) were successfully operated on with the exoscope. In the exoscope group, we observed one minor intraoperative complication. Image quality was deemed inferior as compared to the OM. Familiarization regarding the handling and image quality was required. The exoscope was found to be ergonomically superior particularly in patients operated under local anesthesia. There was a statistically significant difference in mean surgical time, 146 min and 129 min for the exoscope and OM group, respectively.

Conclusion:
Cochlear implant surgery was found to be feasible with a 3D exoscope. However, there is a learning curve to overcome regarding handling and the different quality of the image. While the exoscope cannot currently compete with the OM in terms of image quality, it allows for better ergonomics for the surgeon. It is worth noting that the sample size of this study is small, and further research is needed to fully evaluate the efficacy and safety of using an exoscope for different surgeries in Otorhinolaryngology.

S12 L1 - Identification of Potential Candidates for CI in a large data base of Hearing Aids users

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Cochlear implants are one of the most Successful neuroprosthesis to date
Despite proven safe and effective technology, the numbers of adult benefit from it is very low
One of the reason is a lack of awareness among health professional to identify referral pathway
The goal of the presentation is to provide a description of a large cohort using hearing aids and potential candidate for implant
Total population for screening is 169416 patients
on which 70470 patients get and hearing aids
Potential candidate for CI was defined according to our agency criteria (HAS) patient with word discrimination SRT in quiet > 60 dB with well fitted hearing aids
In this presentation, we describe
1 The percentage of candidate according to BIAP classification
2 Specificity and sensitivity PTA and SRT to identify potential candidate
3The comparison between speech in quiet and speech in noise as a selection criteria for candidacy
4The impact of hearing aid fitting on this candidacy
In this cohort the number of patients who meet the criteria for implantation not referred is over 80%

S12 L2 - Long-term outcome of cochlear implantation in children with cochlear nerve deficiency

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Introduction: Cochlear implantation is well-established and widely accepted as an effective method for auditory rehabilitation in children with severe to profound sensorineural hearing loss. In recent years, the candidacy criteria have been expanded in which children with inner ear malformations with or without cochlear nerve deficiency (CND) or additional disabilities are considered candidates.
Objectives: This study aimed to assess the long-term outcome of auditory performance and speech intelligibility in children with CND who received cochlear implants (CI) in our centre.
Methods: A retrospective review of the UKM Cochlear Implant Program from January 2007 to May 2024 was conducted. Preoperative assessments, including imaging findings (MRI and CT scan), unaided and aided hearing thresholds, were retrieved from the patient database. Outcome measures included aided hearing thresholds with cochlear implants, Categories of Auditory Performance II (CAP II), and Speech Intelligibility Rating (SIR) scores at multiple time points up to 5 years post-cochlear implantation.
Results: Thirteen children with CND, aged between 1 year 4 months and 12 years, were included in this study. On imaging, majority (61.5%) of the cochlear nerve were not visualised at the level of internal auditory canal. Communication modalities varied, with auditory-verbal (23.1%), total communication (53.8%), and sign language (23.1%) being employed. Significant improvements in aided hearing thresholds were observed one year post-implantation, reaching a ceiling effect (20-30 dB HL). CAP II scores demonstrated a statistically significant improvement up to 3 years post-implantation, plateauing thereafter at an average score of 5, indicative of understanding common phrases without lipreading. SIR scores exhibited continued improvement up to 5 years post-implantation.
Conclusion: Cochlear implantation yielded significant benefits for pediatric patients with CND, highlighting the importance of extending access to this transformative technology. Cochlear nerve deficiency on imaging does not exclude the function of residual hearing.

S12 L3 - Cochlear implantation in patients with mumps-related hearing loss

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Objective:
To assess results of CI implantation in subjects with a history of mumps and different duration of hearing loss.
29 patients (13 women, 16 men) aged between 12 and 71 years, mean age 45.2 were included in the study. Patients had sensorineural hearing loss and a history of mumps. The age at the onset of hearing loss was 2–38 years, the duration of hearing loss was 9–63 (M = 33.7; SD = 14.2).
Performed Intervention included minimally invasive cochlear implantation using the round window approach. Pure tone audiometry (125-8000 Hz) was performed preoperatively and monitored for two years postoperatively. Speech understanding was assessed preoperatively and at 18 months postoperatively.

Results:
Mean hearing thresholds across all frequencies were 98.4 dB HL (SD = 13.4) preoperatively and 103.3 dB HL (SD = 10.3) at 12 months postoperatively. Speech understanding assessed before CI implantation in well-fitted hearing aids was on average 2.4% (SD = 8.4), whereas after CI implantation it was on average 71.2% (SD = 17.7) in quiet and 51.7% (SD = 19.1) in noise. The longer the duration of the hearing loss, the worse the speech understanding both measured preoperatively (rho = -0.39; $p < 0.05$) and postoperatively (rho = -0.36; $p = 0.056$ in quiet and rho = -0.38; $p < 0.05$ in noise).

Conclusions:
Early CI implantation is recommended for sensorineural hearing loss caused by mumps.

S12 L4 - Cochlear implantation in syndromic patients: difficulties and lessons learnt

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Objective:
Identify the prevalence of syndromes in a cohort of patients who underwent cochlear implantation, to report on the presence of inner and middle ear malformations and highlight the surgical difficulties encountered.

Study Design:
Observational, retrospective study.

Setting:
Tertiary referral children's hospital pediatric cochlear implant program.

Material and Methods:
An IRB-approved retrospective chart review of children undergoing cochlear implantation at a tertiary academic medical center, Cairo, Egypt, from 2018 to 2023. Preoperative imaging data of syndromic patients in that cohort with special attention to the presence of inner ear or middle ear malformations were collected. Abnormal intraoperative findings and difficulties reported by the surgeons were also noted.

Results:
1024 children were unilaterally implanted for bilateral profound hearing loss. There were 45 cases diagnosed with associated syndromes (4.3%). The commonest syndromes were Jervell and Lange Nielsen (JLN) syndrome followed by Waardenberg syndrome (WS), in a prevalence of 34% and 32% respectively. These syndromes had no associated inner ear malformations (IEM). Less common syndromes included Branchio-oto-renal (BOR) syndrome, CHARGE association and Treacher Collins syndrome, 3 cases each, and keratosis icthyosis deafness syndrome (KID), Usher syndrome and Albino, 2 cases each and an H syndrome case. There were 9 cases (20%) with IEM, with 6 cases of perilymph gusher. Two cases had middle ear anomalies and one case had a facial nerve course abnormality. The outcome of these cases was similar to non-syndromic cases.

Conclusion:
Children with syndromic HL should be dealt with on a case by case scenario to diagnose inner and middle ear malformations. Additional disabilities can affect the rehabilitation procedures.

S12 L5 - Early auditory development of cochlear implanted children with sensorineural hearing loss following congenital CMV infection

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The aim of the study was to assess early auditory development in CI children with CMV-related hearing loss.
The retrospective study included children with congenital CMV who underwent cochlear implantation at an early age due to hearing loss caused by the infection.

Patients:
47 CI children with sensorineural hearing loss following congenital CMV infection with mean age 14 months.
Applied intervantion included minimally invasive cochlear implantation via round window.

Main Outcome Measures:
All children underwent Auditory Brainstem Response test before operation. Early development was assessed with LittleEARS Auditory Questionnaire. The questionnaire was performed at CI activation assessing pre implant auditory development and at each follow up visit related to CI fitting to 14 months of CI use.

Results:
In children with CMV-related hearing loss the mean LittlEARS total score was 5.2 pts. (SD=7.1) at CI activation, 16.7 pts. (SD=8.8) at 5 months of CI use, and 24,8 pts. (SD=8.4) at 14 months after implantation. In the reference group the mean results were as follow: 8.3 pts. (SD=7.6) at CI activation, 25.0 pts. (SD=5.6) after 5 months of CI use, and 32.3 pts. (SD=3.9) 14 months post activation.

Conclusions:
Early cochlear implantation in children with sensorineural hearing loss following congenital CMV infection facilitates their early auditory development. Nevertheless in this group of children the level of auditory development is lower comparing to the level observed in children with no CMV-related hearing loss.

S12 L6 - Outcomes of cochlear implantation compared to auditory brainstem implantation in cochlear nerve deficiency

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Introduction:
Cochlear nerve deficiency is a recognized cause of congenital sensorineural hearing loss, presenting a complex challenge in managing hearing impairment in affected children. The absence or underdeveloped cochlear nerve hinders effective electrical stimulation, impacting signal transmission to the brainstem and auditory cortex. Additionally, cochlear nerve deficiencies often coexist with other inner ear malformations, potentially complicating cochlear implant success in pediatric cases. Building on positive outcomes observed in adults undergoing auditory brainstem implantation (ABI), there has been an extension of candidacy to pediatric populations previously deemed unsuitable for cochlear implants (CIs).

Objective:
This study aims to compare the outcomes of cochlear implantation and auditory brainstem implantation in children with diverse auditory nerve conditions.

Methods:
A retrospective chart review included two pediatric groups: seven recipients of ABIs with cochlear nerve aplasia and another seven children with cochlear nerve deficiencies who underwent CI surgery. Auditory skills and speech outcomes were evaluated using various tests from the Evaluation of Auditory Responses to Speech (EARS) test battery.

Results:
Individual outcome variations were observed based on the auditory nerve status. The ABI group demonstrated a mean CAP score of 2.87 and a mean SIR score of 0.62. In contrast, the CI group exhibited a mean CAP score of 1.29 and a mean SIR score of 0.42.

Conclusion:
Our findings align with existing literature on auditory perception, speech, and language development outcomes in pediatric auditory brainstem implantation. This study contributes to the growing body of evidence emphasizing the crucial role of determining cochlear nerve status in the surgical decision-making process for these pediatric populations.

S12 L7 - International consensus on intraoperative testing for cochlear implantation & the recommended minimum intraoperative testing battery

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Introduction:
In cochlear implantation surgery there are a wide variety of intraoperative tests available. However, no consensus exists on which tests constitute the minimum necessary battery. Toward this end, we assemble an international panel of clinical experts to develop, refine, and vote upon a set of core consensus statements. Moreover, we have studied the usage patterns, recommendations, and attitudes of practitioners toward intraoperative testing.

Methods:
For statement evaluation and refinement, we employed a modified Delphi consensus panel structure. Multiple interactive rounds of voting, evaluation, and feedback were conducted to refine statements and achieve convergence on a set of consensus statements.
Furthermore, survey was developed and administered to a group of practitioners (n=34). We assessed practitioners' patterns of usage among fourteen different intraoperative tests, and their recommendations of a minimum battery, as well as broader statements about the utility and purpose of different tests.

Results:
Twenty-nine provisional statements were included in the original draft. After completing all three rounds, consensus was reached on twenty-five of these.
The survey results showed that respondents varied widely in both the number and types of tests they employed, both in routine and in special cases. The most frequently recommended tests for a minimum battery were facial nerve monitoring, electrode impedance measurements, and evoked compound action potentials (ECAPs). The perceived value and influence upon surgical decision-making also varied, with high-resolution CT being rated the highest on both measures.

Conclusion:
A final core set of twenty-five consensus statements were generated, covering wide areas of intraoperative testing during CI surgery. These statements may provide utility as evidence-based guidelines to enhance the quality and uniformity of surgical practice.
Moreover, Facial nerve monitoring, electrode impedance measurements, and ECAPs are the recommended intraoperative test battery for cochlear implantation surgery.

S13 L1 - Facial functional electrical stimulation to prevent denervated muscle atrophy in patients with facial paralysis - the road to clinical routine

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Denervation in patients with severe facial paralysis lead to facial muscle atrophy. The functional deficits and the facial disfigurement represent main issues for the patient's quality of life. The muscle atrophy can be transient and regress in case of regeneration of the facial nerve or permanent if the nerve cannot regenerate. In a series of clinical studies in the last years, we have systematically analyzed the effects of modern facial functional electrical stimulation (F-FES) to prevent muscle atrophy in patients with transient facial paralysis or to prevent the progression of the atrophy in patients with permanent facial paralysis.
First, we have developed standardized protocols to stimulate denervated facial muscles, as stimulation of denervated muscles is much different from stimulation of innervated facial muscles. There are some reservations in the facial nerve community about F-FES based on outdated, less valid small case series. Therefore, we showed, as a second step, that F-FES is well tolerated by the patients, has no major side effect, and most important, does not hinder or deteriorate facial nerve regeneration. Third, we have established a protocol for a home-based training allowing the patient to perform effective F-FES in addition to all the usual standard rehabilitation procedures like for instance physiotherapy. Finally, we have we have just completed a prospective clinical study showing the effectivity of F-FES to prevent muscle atrophy in patients with facial paralysis based on standardized and validated outcome measures: facial nerve grading, automated facial imaging analysis, facial specific patient-reported outcome measures, and facial muscle ultrasound.
Now it is time to bring modern F-FES on the road to clinical routine. We will know start to build an network of facial nerve centers to validate F-FES on an international and multicenter level and to develop clinical guidelines for an optimal use of F-FES for patients with facial paralysis.

S13 L2 - Tinnitus in patients with orofacial complaints

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Introduction:
Somatosensory tinnitus is a clinically significant subset of chronic tinnitus. The frequent co-occurrence of orofacial pain and tinnitus has led to the assumption that there may be a link between these two conditions. This study investigated the prevalence of subjective tinnitus in a population referred to the Department of Orofacial Pain at the Center for Dental Medicine of the University of Zurich. The aim of this study was to investigate the correlation between orofacial complaints and tinnitus manifestation, considering sociodemographic parameters.

Methods: For the analysis, anonymized data sets of 1369 people who visited the clinic between 2017 and 2020 were extracted from a web-based interdisciplinary symptom evaluation (WISE) tool. The severity of tinnitus, the frequency of tinnitus and the duration of ear complaints were evaluated and correlated with orofacial complaints.

Results: The majority of the 1369 patients who participated in the WISE survey due to orofacial complaints were female (69%). 27.5% of the 1369 patients suffered from their orofacial main complaints between six months and two years. Of the 1369 patients, 19.7% (269 patients) gave a positive response regarding ear complaints and therefore had to complete the Tinnitus Handicap Inventory 12 (THI-12) questionnaire. The majority of these patients were female (62.1%). The average THI-12 score for women was 9.3 points and for men 11.6 points, with a maximum possible score of 24 points. The highest frequency of tinnitus in women, measured against the total female population, was found in the THI-12 subgroup "no impairment" at 7.5%. The highest frequency of tinnitus in men (8%) was found in the "severe impairment" tinnitus group. Thus, the men in this study were more frequently affected by tinnitus than the women.
According to the Spearman correlation test, the THI-12 questionnaire correlates positively with all other questionnaires used in the WISE questionnaires, including pain, anxiety, depression, health, stress and insomnia. The strongest correlation was found between the THI-12 and the Patient Health Questionnaire 4 (PHQ4) ($p = 0.510$).

Conclusion: In our study, we were able to show that the co-occurrence of orofacial complaints and ear complaints, such as tinnitus, is a relatively common event. According to our study, the co-occurrence of severe tinnitus and orofacial pain is more common in men than in women.

S13 L3 - Tinnitus and GABA receptors in the auditory cortex: a PET study

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Aim of the study:
Subjective tinnitus is a common condition, which is believed to be based on altered spontaneous activity in auditory structures in the brain. Animal studies show that decreased GABA, the main inhibitory neurotransmitter in the brain, can lead to a hyperactivity of central auditory neurons and to tinnitus. Furthermore, MR spectroscopy measurements suggests a decreased concentration of GABA in the auditory cortex in humans. In order to further investigate the role of GABA in tinnitus at a molecular level, the current study aims to measure GABA receptors in the brain and compare people with and without tinnitus.

Methods:
The study included three groups of participants: (1) Healthy people without tinnitus and with good hearing, (2) Hearing-impaired people without tinnitus, (3) Hearing-impaired people with tinnitus. In order to measure GABA receptor density, positron emission tomography (PET) was performed in all participants, using an 11C-Flumazenil tracer.

Results:
A preliminary analysis showed a pronounced increase of receptor availability in the auditory cortex of participants with tinnitus as compared to participants without tinnitus. A similar effect was not observed in non-auditory brain structures such the calcarine sulcus and cuneus which have a visual function.

Conclusion:
The PET scans identify GABA receptors that are not occupied by GABA. The results showed that tinnitus is associated with a surplus of unoccupied GABA receptors, specifically in the auditory cortex. This may be due to a reduced GABA concentration as observed in MR spectroscopy. Also, it could represent a homeostatic response of auditory cortex neurons, where cells overexpress GABA receptors to mitigate hyperactivity. These results underline the key role of GABAergic inhibition in tinnitus. They may strongly promote the search for a pharmaceutical intervention for tinnitus. Furthermore, the PET scan technique applied here, may provide a robust objective biomarker for what is usually referred to as subjective tinnitus. In other words, the term 'subjective tinnitus' may soon become obsolete due to this objective method.

S13 L4 - Development and Validation of an Outcomes Measure for the Hearing-impaired Children and Parents

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Objectives: Self-reported hearing-specific instruments can complement traditional hearing tests as they provide valuable information regarding how hearing impairments or interventions affect everyday life. To assess binaural hearing benefits, two questionnaires were developed for evaluating spatial hearing ability and hearing in difficult situations: the Speech, Spatial, and Qualities of Hearing Scale (SSQ; (Gatehouse & Noble, 2004). In this study we translate and validate the Mandarin Chinese version of the Speech, Spatial, and Qualities of Hearing Scale (SSQ) for children with hearing impairment (C-SSQ-C) and for their parents (C-SSQ-P).

Methods: We translated the SSQ for children into Mandarin Chinese and verified its readability and comprehensibility. A total of 105 participants with moderate to profound hearing loss and 54 with normal hearing were enrolled in the validation process. The participants with HL were fitted with bilateral hearing aids, bimodal hearing, or bilateral cochlear implants. The C-SSQ-P was administered to the parents of participants aged 3 to 6.9 years, and the C-SSQ-C was administered to participants aged 7 to 18 years. The internal consistency, test–retest reliability, and validity were evaluated for both questionnaires.

Results: Both C-SSQ-P and C-SSQ-C demonstrated high internal consistency (Cronbach's alpha > 0.8) and good validity [generalized linear model revealed significant negative relationships between the C-SSQ-P subscales with aided better hearing threshold (β = -0.08 to -0.12, $p \leq 0.001$) and between the C-SSQ-C subscales with worse hearing threshold (β = -0.13 to -0.14, $p < 0.001$)]. Among the children with hearing loss, the participants with bilateral cochlear implants had demonstrated better performance than those with bimodal hearing and bilateral hearing aids, as evidenced by the highest mean scores in 3 subscales.

Conclusions: Both the C-SSQ-P and C-SSQ-C were found to be reliable and valid questionnaires for children and adolescents with HL. The C-SSQ-P can be used in evaluating young children aged 3 years or older after 7 days of observation, whereas the C-SSQ-C can be administered for children aged 7 years or older who can provide ratings for themselves, although some may require assistance from their parents depending on their reading and comprehension abilities. Both questionnaires correlate with (aided-) hearing thresholds, highlighting their potential for use in monitoring the benefits of HAs and CIs.

S13 L5 - Premature test termination in a German matrix speech test in noise

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Background:
Speech reception thresholds (SRTs) in noise can be estimated with speech in noise tests using adaptive procedures. The most frequently used class of tests for this purpose are matrix-tests, which are available in several languages.

Method:
Since these tests are time-consuming, it is preferable to use as few trials as possible to identify reliable results. In this study, we retrospectively evaluated clinical records of matrix sentence tests from cochlear implant patients (N = 789 tests) and simulations thereof to investigate the effect of a premature test termination on SRT assessment. In addition, the adaptive test data were fitted with a psychometric function to the test track to determine its reliability.

Results:
Terminating the clinical tests after 20 trials instead of 30 trials would have shortened the testing time by 1.4 minutes on average. The deviation of the two SRTs was 1 dB or higher in 7.9% of the tests. For clinical data and simulation results, the deviation increased with increasing SRTs. Fitting a psychometric function resulted in accurate thresholds which correlated very well with the conventionally calculated results (intra-class correlation coefficient (ICC) = 0.99).

Discussion and Conclusions:
The agreement of the test results after 20 and after 30 trials is high and for the majority of the tested patients trials 20 trials would have produced reliable results. However, clinical data and simulation results agree that for poor performing listeners the deviations can become considerable. We therefore recommend the reduction of the number of trials only for listeners with a relatively good speech understanding, i.e. achieving negative SRTs in the first 20 test items.

S13 L6 - Influence of simulated adverse events of the Floating mass transducer in a mechanical middle ear model

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Introduction: The Floating Mass Transducer (FMT) of the Vibrant Soundbridge (VSB, Medel, Innsbruck, Austria) provides several coupling options for the stimulation of the ossicular chain. Direct comparison of the same couplers in clinical trials is not possible but laser Doppler vibrometry (LDV) in cadaveric human temporal bones is widely used for this purpose [1, 2]. However systematic validation of several implantation parameters is difficult because any manipulation can irreversibly deteriorate the transfer function of the middle ear response. Using a mechanical middle ear model may facilitate systematic evaluation e.g for impaired coupling.
In this study we compared the vibratory output of the FMT of the VSB with three different couplers (short process (SP), long process (LP) and a modified long process (modLP)) in an acoustic-mechanical middle ear model (AMEM) with focus on the influence of impaired FMT coupling on the transfer function.

Methods: The AMEM consists of artificial real size ossicles which all have a physiologic mass. We used 50 logarithmic sinus stimuli between 100 to 8000 Hz either applied by a loudspeaker in the external auditory canal or the implanted FMT using couplers. We additionally simulated different potential impairments of the FMT transmission properties i.e. unwanted contact to surrounding structures, load or tension on the cable and reduced crimping. The vibration of the stapedial footplate was measured with a single point LDV.

Results and Discussion: For acoustic stimulation, the transfer function of the stapes motion was within the ASTM for most frequencies. In the frequency range between 700 and 1000 Hz the magnitude exceeded the ASTM standard. A passive FMT (no electrical stimulation) resulted only in minor changes.
The comparison of the different couplers in normal condition showed similar results to Graf [1] with a benefit of the SP coupler in frequencies higher than 1000 Hz and a benefit of the LP coupler in a small frequency range at approximately 500 Hz. A contact of the FMT to a solid structure reduced the magnitude with the SP, LP, modLP coupler by maximally 15, 25 and 20 dB respectively. In case of a stress on the FMT cable, magnitude changes are also more distinct for the LP coupler than for the modLP and the SP couplers. Crimping of the SP coupler with only two instead of four legs resulted in an additional single spike in magnitude with a small frequency shift but generally the same magnitudes. On the other hand off-axis crimping of the LP coupler reduced the magnitudes by 15-20 dB for frequencies around 1000 Hz.

Conclusion: Our investigations in the mechanical middle ear model showed that the

SP coupler is more robust to simulated implantation related impairments of the FMT that the LP couplers.

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S13 L7 - Better understanding of surgical video of mastoidectomy by Video inpainting and Stabilization using artificial intelligence

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Background and Objective:
Optimizing the educational experience of trainees in the operating room is important; however, ear anatomy and otologic surgery are difficult for trainees to grasp. While viewing otologic surgery, video quality has limitations, such as visual disturbance and instability. We aimed to (1) improve the quality of surgical video (tympanomastoidectomy) by employing artificial intelligence (AI) techniques and (2) ask trainees about the effectiveness of processed videos via questionnaire-based evaluation.

Methods:
We conducted prospective studies using video inpainting and stabilization techniques processed by AI. In each study set, we enrolled 21 trainees from a tertiary referral center, asked them to watch processed videos, and completed questionnaires composed of 6 checklists scored from +2 (helpful) to -2 (bothersome).

Results:
Surgical videos with the video inpainting technique via implicit neural representation model were found to be the most helpful for medical students (0.79 ± 0.58), followed by high-grade residents (0.47 ± 0.21), low-grade residents (0.45 ± 0.26), and fellows (0.04 ± 0.33). Video inpainting was particularly helpful in identifying bleeding focus. Videos with the stabilization technique via point feature matching were found to be the more helpful for low-grade residents (0.91 ± 0.12) and medical students (0.78 ± 0.35), followed by high-grade residents (0.68 ± 0.31) and fellows (0.33 ± 0.17). Video stabilization was helpful in overall visuality and understanding of surgical procedures.

Conclusions:
Surgical videos using video inpainting and stabilization techniques with AI were helpful and promising for educating trainees, especially participants with less anatomical knowledge and surgical experience. Video inpainting was the most helpful in identifying bleeding focus, and video stabilization was beneficial in overall visuality and understanding of surgical procedures.

S14 L1 - Cognitive impact of hearing loss in absence of language

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Hearing loss in childhood has far-reaching medical, social and educational consequences. Currently, access to hearing is, as a rule, provided in the second and the third year of life, which allows the acquisition of spoken language, but is still too late for unlocking the full developmental potential of the brain. While bilaterally children implanted in the first 24 months perform at age-appropriate level at 5.0-7.5 years, earlier implantation within this time provide better outcomes (Illg et al., 2024, J Speech Lang Hear Res). The connectome model of deafness suggests the impact of deafness on cognitive function (Kral et al., 2016, Lancet Neurol). So far it remained unclear whether the cognitive impact of hearing loss is related to hearing loss or whether these can be explained by consequences of hearing loss on language.

Here we demonstrate that developmental hearing loss in animal models (in absence of language) increases impulsiveness, play fighting and negatively affects learning (Jelinek et al., 2023, Curr Res Neurobiol). Even with deafness induced in adult rats (Johne et al., 2022, Front Neurosci; Land, Stenzel, Mesbah, Johne, Baumhoff, Konerding, Schwabe, Kral, unpublished) caused deficits in conceptual learning and impacted on the speed of adaptation to visual tasks, while final best performance did not differ between the hearing and deafened group. Deafened animals additionally showed increased forgetting and faster retrieval of rewards. Recordings using multielectrode arrays in visual, auditory and prefrontal cortex of deafened animals (compared to normal hearing controls) demonstrated alterations of activity related to visual and auditory stimulus processing. Therefore, hearing loss affects the physiology of executive functions and the link between sensory cortex and prefrontal cortex. Also, crossmodal reorganization was observed in these animals (review in Kral and Sharma, 2023, Trends Neurosci). In conclusion, hearing loss directly affects cognitive function even in absence of language-related effects. In children, appropriate cortical development requires hearing and active communication with a social partner in the first months of life, when synaptic development in the auditory cortex is controlled by sensory input. This has downstream consequences on cognitive function.

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S14 L2 - How the gut microbiome can influence hearing? New insight on a gut-cochlear axis

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Recent advances in neuroscience have revealed a bidirectional communication between the gut microbiota and the central nervous system (CNS), known as the "gut–microbiota–brain axis." Imbalance in the gut microbiota, called dysbiosis, can increase intestinal permeability, allowing pathogens to trigger inflammation in distant organs. Despite these established connections, no research has explored the link between gut microbiota alterations and inner ear function. To address this gap, this study delved into the molecular mechanisms underlying a potential association between gut microbiota alterations and sensorineural hearing loss (SNHL). To this aim, we used a mouse model of gut dysbiosis induced by dextran sulfate sodium (DSS) treatment, supplemented with fecal microbiota transplantation (FMT) from donor patients with active (aUC) or remissive (rUC) ulcerative colitis. This enabled us to exacerbate or ameliorate the microbiome imbalance, respectively. Auditory brainstem responses (ABRs) were conducted alongside morphological, immunofluorescence, and molecular analyses. ABR results revealed a significant increase in auditory thresholds in mice subjected to DSS and FMT-aUC treatments. Conversely, FMT from rUC donors exhibited a protective effect on auditory function, highlighting the beneficial impact of microbiota restoration. Morphological evaluations revealed loss of outer hair cells (OHCs), degeneration of spiral ganglion neurons (SGNs), and atrophy of the stria vascularis in mice with gut dysbiosis. Conversely, FMT from rUC donors displayed a protective effect on cochlear structures. Immunofluorescence and Western blot analyses unveiled increased oxidative stress and inflammation in cochlear tissues of mice with gut microbiota alterations, while restoration of microbiota composition exerted otoprotective effects. These findings were associated with disruptions in the integrity of the blood-labyrinth barrier (BLB), characterized by altered expression of tight junction proteins (ZO-1 and Occludin), Na+/K+-ATPase levels, along with increased of pericytes damage and vascular permeability in mice with altered microbiota composition. Overall, these results suggest a mechanistic link between gut microbiota alterations and SNHL through oxidative stress and inflammation mediated by changes in BLB permeability. This study provides experimental evidence supporting the existence of a gut-cochlear axis and highlights the potential therapeutic implications of restoring gut microbiota balance in mitigating hearing impairment associated with gut dysbiosis.

***S14 L3* - Desynchronization of auditory development from sensory and motor systems in the first years of life of a deaf baby: Cochlear implant at nine months may not be early enough**

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Early diagnosis of hearing loss at birth, early fitting of hearing aids before six months of age, and early cochlear implantation (CI) by 9-10 months of age are considered the most important factors affecting language development in children with CI. Nonetheless, there is still much-unexplained variance in the language skills and cognitive abilities of these children, even when no other risk factors for developmental delays are present beyond hearing loss. The extent of this unexplained variance (40-50%) in language abilities of CI users is considerably higher compared to the expected variance in typically developing children. One possible unexplored explanation is that, for most profoundly deaf children with CI and in the best case scenario, functional hearing does not occur before nine months of age. It is suggested that sensory deprivation in one modality results in its developmental desynchronization from other modalities involved in active communication, such as vision, touch, and the motor system. This desynchronization is crucial because, in normally hearing (NH) children, a plethora of developmental processes involving multimodal inputs—including eye gaze, facial expressions (e.g., smiles), hearing and hand gestures—take place simultaneously within the first months of life. These multimodal inputs are part of the adult communication cycle and are essential for establishing early multisensory and motor integration of neural circuits. Thus, we hypothesize that the current habilitation practices for children with CI may be too late and insufficient to prevent the desynchronization of auditory development from sensorimotor, cognitive, and linguistic development, affecting multimodal representations. This desynchronization may ultimately contribute to poor language outcomes and deleterious consequences for cognitive development. The presentation will discuss: (1) neurophysiological evidence related to multimodal interaction and the development of brain connectivity; (2) multimodal communicative behaviors in NH children in the first year of life and their importance for language development; and (3) what can be done to promote the development of age-appropriate functional connectivity of language and cognitive networks in deaf infants.

S14 L4 - Machine learning-based longitudinal prediction for GJB2-related sensorineural hearing loss

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Background:
Recessive GJB2 variants, the most common genetic cause of hearing loss, may contribute to progressive sensorineural hearing loss (SNHL). The aim of this study is to build a realistic predictive model for GJB2-related SNHL using machine learning to enable personalized medical planning for timely intervention.

Method:
Patients with SNHL with confirmed biallelic GJB2 variants in a nationwide cohort between 2005 and 2022 were included. Different data preprocessing protocols and computational algorithms were combined to construct a prediction model. We randomly divided the dataset into training, validation, and test sets at a ratio of 72:8:20, and repeated this process ten times to obtain an average result. The performance of the models was evaluated using the mean absolute error (MAE), which refers to the discrepancy between the predicted and actual hearing thresholds.

Results:
We enrolled 449 patients with 2,184 audiograms available for deep learning analysis. SNHL progression was identified in all models and was independent of age, sex, and genotype. The average hearing progression rate was 0.61 dB HL per year. The best MAE for linear regression, multilayer perceptron, long short-term memory, and attention model were 4.42, 4.38, 4.34, and 4.76 dB HL, respectively. The long short-term memory model performed best with an average MAE of 4.34 dB HL and acceptable accuracy for up to 4 years.

Conclusions:
We have developed a prognostic model that uses machine learning to approximate realistic hearing progression in GJB2-related SNHL, allowing for the design of individualized medical plans, such as recommending the optimal follow-up interval for this population.

S14 L5 - Interpretation of psychophysical tests from computational models

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Background: Acoustic information is represented distinctly different on the auditory nerve in the implanted and normal hearing ear. While single-fiber experiments offer insights into these representations, they are not feasible in humans. Psychophysical tests, designed to probe specific auditory functions, also facilitate comparisons between normal and electric hearing. Recent computational advances have enabled the simulation of neural responses in the cochlea. However, bridging the gap between these simulated responses and human psychophysical performance necessitates an interpretation model. This research explores the utility of such models in mimicking the results of psychophysical tests, potentially offering insights into signal processing algorithms for cochlear implants.

Methods: We simulated neural activation using models for normal hearing (Bruce 2018, Hearing Research) and the implanted ear (Kalkman et al. 2022, Hearing Research; Van Gendt et al. 2020, Hearing Research) in response to various test stimuli, including masker-probe, amplitude modulation, and spectrally modulated ripple test (SMRT). Information at the fiber level was consolidated into critical bands and augmented with noise to align model performance with empirical data. The processed signals were then used in interpretation models to predict outcomes in a 3-alternative forced-choice test paradigm.

Results: Adjusting noise levels allowed us to replicate psychometric curves for simpler tests, such as the masker-probe and amplitude modulation tests. However, the SMRT, which involves complex temporal and spectral changes, posed significant challenges. The interpretation models struggled to generate realistic psychometric curves for the SMRT, with the signals either being too similar or distinctly differentiable. Despite these challenges, the models successfully identified various effects documented in auditory research.

Conclusion: Combining electric and acoustic models yields valuable insights into the stimulation patterns of psychophysical tests. Interpretation models mimic human behaviors in simpler tests effectively, but fail to replicate clinical outcomes for more complex tests when analysis across the full spectrum of critical bands are required. This underscores the complexity of neural processing beyond the auditory nerve and the need for refining interpretation models to better understand auditory perception.

S14 L6 - Hearing Health Strategy: the Hearing Health Forum EU Manifesto

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Introduction: In the European Union (EU), it is estimated that 34.4 million adults live with a disabling hearing loss affecting all ages and these figures will rise as our population ages. Hearing loss is the 4th leading cause of disability globally.
People living with hearing loss experience psychological distress, suffer from social isolation, discrimination and stigma. It became apparent that hearing loss is the number one modifiable risk factor for dementia.
Moreover, hearing loss and its comorbidities lead to €213 billion direct costs (medical expenses) and indirect costs (impact on the economy) for European governments.
Yet two out of three persons with hearing loss do not have access to hearing care, treatment, or rehabilitation.
However currently, hearing health policies are rare across Member States.
Methods and aim: A broad consultation and discussions were performed with many stakeholders and organisations by the Healing Health Forum EU partnership (HHF EU) (www.hearinghealth.eu/hearing-loss-manifesto) in order to **to place patient-centered hearing health high on the policy agenda by the European Commission** and the EU policy stakeholders, to ensure that persons living with hearing loss have equal access to care, and to mitigate the wider impact on Europe's economy and societies by launching a European Hearing Health Strategy, reflecting the policy framework already developed by the World Health Organization (WHO) for hearing.
Results, discussion and actions: We identified 4 pillars to focus on Hearing Health Strategy:

- **H**earing loss awareness: raise awareness of hearing loss and educate populations to reduce stigma and promote social inclusion.
- **E**arly prevention: strategies are put in place at the national level to ensure prevention and detection of hearing loss.
- **A**ccess and care: facilitate access to hearing healthcare, interventions, treatment options, and rehabilitation for persons living with hearing loss.
- **R**esearch: the collection of data to facilitate evidence-based policymaking for persons living with hearing loss.

Conclusion: Launching a European Hearing Health Strategy focused on the HEAR pillars will achieve political alignment and guide Member States in the cost-effective development and implementation of policies to tackle the impact of untreated hearing loss. This strategy would highlight the EU's commitment to build a Health Union inclusive of all its citizens, including those experiencing hearing loss.
(www.hearinghealth.eu/hearing-loss-manifesto)

S15 L1 - Clinical development of AK-OTOF gene therapy for *OTOF*-mediated hearing loss

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Background: The otoferlin gene (*OTOF*) encodes otoferlin, a protein critical for signaling at the inner hair cell synapse; individuals with mutations in *OTOF* typically present with Severe to Profound hearing loss. Recent gene therapy and intracochlear delivery support the potential to restore hearing in individuals with *OTOF*-mediated hearing loss using a one-time, local administration of AK-OTOF (AAVAnc80-hOTOF). A phase 1/2 clinical trial (NCT05821959) has been initiated to assess the safety, tolerability, and bioactivity of escalating doses of AK-OTOF in children with Profound hearing loss due to *OTOF* mutations.
Methods: Nonclinical studies in otoferlin knock-out mice and primates evaluated the delivery of genetic medicines to the inner ear, including the development of a dual adeno-associated viral vector encoding full-length human otoferlin, a delivery device, and an intracochlear administration procedure. These studies formed the design of the clinical investigation of AK-OTOF, evaluation of intervention window, identification of biologically active dose levels, assessment of onset and durability of functional recovery, and evaluation of safety. Participants in the AK-OTOF-101 Clinical Trial have Profound hearing loss at baseline and receive, via a minimally invasive external auditory canal approach, a single intracochlear administration of AK-OTOF in one ear; participants in the first cohort receive AK-OTOF at a dose of 4.1E11 total vector genomes. Hearing restoration is assessed by behavioral audiometry and BERA.
Results: Administration of AK-OTOF to NHPs and otoferlin knock-out mice results in robust expression of full-length otoferlin, with restoration of auditory function. Safety data demonstrate AK-OTOF was systemically and locally well tolerated, with no adverse effects related to AK-OTOF, including in clinical pathology, otic or systemic histopathology, or cochlear and auditory function. In the AK-OTOF-101 Clinical Trial, the first participant, an 11-year-old with Profound congenital hearing loss, experienced restored hearing within 30 days of AK-OTOF administration, achieving thresholds of 65 to 20 dB HL. The surgical administration procedure and the product candidate were well tolerated, and no serious adverse events occurred. Safety and efficacy data from participants receiving AK-OTOF prior to January 2024 will be presented.
Conclusions: The AK-OTOF preclinical development strategy, leading to an interventional clinical trial in children with *OTOF*-mediated hearing loss, can serve as an exemplary path to achieving the broader goal of developing precision genetic medicines with the potential to restore, improve, and preserve high-acuity physiologic hearing.

***S15 L2* - The Phoenix platform as novel tool to unveil regenerative pathways in presenescent auditory neuroprogenitors**

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Hearing loss affects over 466 million people worldwide and is a major socioeconomic burden. Both genetic and environmental factors (i.e. noise overexposure, ototoxic drug treatment or ageing) promote irreversible degeneration of cochlear hair cells and associated auditory neurons, leading to sensorineural hearing loss. In contrast to birds, fish or amphibians, the mammalian inner ear is virtually unable to regenerate due to the limited stemness of auditory progenitors and no causal treatment is able to prevent or reverse hearing loss.
We have previously identified and characterized the phoenix auditory neuroprogenitors (ANPGs) as highly proliferative progenitor cells isolated from the cochlea of a specific strain, called A/J mouse. These ANPGs have a virtually unlimited capacity to self-renew >40 generations. In the present study, we aimed at identifying signaling pathways responsible for the intrinsic high stemness of phoenix ANPGs. A transcriptomic comparison of traditionally low stemness ANPGs, isolated from C57Bl/6 mice and high stemness phoenix ANPGs from A/J mice was performed. Based on the differentially expressed pathways, we reprogrammed low-stemness ANPGs with a strategic pharmacological combination of a WNT agonist and TGFβ/Smad inhibitors, which resulted in a remarkable increase in the growth of presenescent neurospheres, effectively allowing the expansion of ANPGs on an extensive scale. The so-called stemness-induced ANPGs exhibited the unique property of being freezable and thawable, facilitating their distribution to other research facilities. Importantly, even after more than 20 generations, stemness-induced ANPGs retained their capacity to differentiate into electrophysiologically active type I-like auditory neurons.
Both the stemness-induced and phoenix ANPGs represent a significant breakthrough in addressing a major bottleneck in auditory research. They offer an efficient, high-throughput, cost-effective, and 3R compatible approach for in vitro screening of potential otoprotective and otoregenerative drug candidates. This study may also open new avenues in the field of inner ear regeneration.

S15 L3 - Exploring Hereditary Deafness: Unveiling Insights with Human-Induced Pluripotent Stem Cells

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The intricate process of inner ear development entails numerous complex and closely coordinated steps, including the proliferation and commitment of otic progenitor cells to become sensory epithelial hair cells and supporting cells. This process is primarily governed by the precise spatio-temporal regulation of gene expression. Given this developmental complexity, gene mutations, such as transcription factors, ion channels, and ciliary proteins, can disrupt inner ear development, leading to hearing loss. Indeed, many gene mutations have been identified in individuals with profound sensorineural hearing loss.

In the context of understanding deafness, our research demonstrates the practical utility of human induced pluripotent stem (hiPS) cells derived from both healthy individuals and patients. We successfully generated hiPS cells from patient fibroblasts, which were then rigorously validated both in vitro and in vivo. Employing a 3D protocol, we produced inner ear organoids and observed that healthy and pathological hiPSCs could give rise to a population of otic progenitor cells capable of differentiating into hair cells (HCs), supporting cells, and neurons. Utilizing this model, we characterized the proliferative capacity, differentiation potential, and cell death dynamics in normal and pathological organoids. This novel human-derived organoid model not only offers valuable insights into the molecular mechanisms underlying pathological inner ear development but also holds promise for future therapeutic interventions.

S15 L4 - Preservation of Residual Hearing and Enhancing Cochlear Implant Outcomes with Drug Y: A Novel Approach to Otoprotection and Neurite Outgrowth

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Background: Cochlear implants (CIs) are commonly used to provide auditory rehabilitation to individuals with severe to profound hearing loss. However, CI leads to electrode induced trauma (EIT) in the inner ear resulting in loss of residual hearing. The preservation of residual hearing following cochlear implantation is crucial for optimizing auditory outcomes and enhancing the quality of life for recipients. Preserving residual hearing will expand indication of CI, increase patient self-confidence and safety when device off. It also allows individuals to benefit from an electric acoustic stimulation device, facilitating better speech perception, especially in noisy environments, and preserving the natural tonal quality of sounds. Molecular mechanisms contributing to the loss of residual hearing post-implantation often involve trauma-induced apoptosis of hair cells, inflammation, and neuronal degeneration. In addition, there is a need for improved interfaces between the CI and auditory neurons. The objective of this study was to investigate the efficacy of a novel Drug Y in preventing apoptosis, reducing inflammation, and improving the neural-electrode interface by promoting neurite outgrowth, thereby preserving residual hearing, and enhancing auditory outcomes in implanted individuals.

Methods: This study utilized *in vitro,* and *ex vivo* models to investigate anti-apoptotic, anti-inflammatory and neuritogenic properties of Drug Y. Various assays measured cell apoptosis, pro-inflammatory cytokine production (TNF-alpha, IL-6), and neurite outgrowth. Additionally, the safety and toxicological profiles of Drug Y were assessed through systemic and local administration in rat model, with auditory brainstem response (ABR) thresholds serving as indicators of hearing preservation. In addition, cochleae were subjected to histopathological examination and confocal microscopy to evaluate for apoptosis.

Results: Drug Y significantly reduced the production of pro-inflammatory cytokines and induced neurite outgrowth in response to lipopolysaccharide stimulation. In an *ex vivo* model of CI trauma, Drug Y significantly prevented hair cell loss and inhibited cleaved caspase activity, indicative of its anti-apoptotic properties. Safety studies confirmed no adverse effects on hearing thresholds or cochlear histopathology.

Conclusions: Drug Y demonstrates significant potential in providing otoprotection for CI trauma. The potential clinical applications of Drug Y extend beyond basic

neuroprotection, as it also offers anti-apoptotic and anti-inflammatory benefits. These findings suggest that Drug Y could serve as a novel therapeutic agent in enhancing CI technology by not only protecting auditory neurons but also by improving the fidelity of signal transmission and overall auditory function. Future studies are warranted to assess efficacy of Drug Y in preclinical animal models tests of cochlear implantation and to determine pharmacokinetic profile. Furthermore, there is a need to explore the underlying molecular mechanisms through which Drug Y confers its protective effects which will promote its translation from bench to bedside. The ultimate goal is to incorporate Drug Y into a second generation of drug-eluting electrodes, paving the way for enhanced CI strategies tailored to individual needs based on specific auditory pathologies.

S15 L5 - The Varieties of Otoferlin-related Phenotype

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Background: Congenital profound hearing loss with preserved cochlear outer hair cell activity (otoacoustic emissions, cochlear microphonic) is the most common phenotype associated with mutations in the *OTOF* gene. Nevertheless, some missense mutations have been associated with a temperature-sensitive phenotype, while few have been found in patients with progressive hearing loss. In this study we report the audiological and electrophysiological findings collected in a cohort of patients carrying two mutant alleles in the *OTOF* gene.
Materials and Methods: Hearing function was evaluated in 16 patients, 13 children (2-36 months) and 3 adults (22-47 years), all carrying pathogenic biallelic *OTOF* mutations. They underwent audiometric assessment with pure tone and speech perception evaluation, and distortion product otoacoustic emissions (DPOAEs) and auditory brainstem response (ABR) recording. Moreover, cochlear potentials were obtained through transtympanic electrocochleography (ECochG) in response to 0.1 ms clicks at intensities from 120 to 60 dB SPL.
Results: Ten children had profound deafness, while 6 subjects, 3 adults and 3 children, had stable mild-to-moderate hearing loss associated with severe impairment of speech perception and delay in language development. All the sixteen patients had absent ABRs, whereas DPOAEs were recorded in all but one subject, including the three adults. Follow up of OAE recordings was available for 7 children, who still showed preserved OAE responses at ages of 5-16 years.
ECochG recordings showed cochlear microphonics and summating potentials with normal latency and peak amplitude, consistently with preservation of both outer and inner hair cell activity. In contrast, the neural compound action potential recorded in normally hearing controls was replaced by a prolonged, low-amplitude negative response. No differences in cochlear potentials were found between *OTOF* patients showing mild or profound hearing loss.
Discussion and Conclusion: These findings suggest that the phenotype of patients carrying mutations in the *OTOF* gene may vary according to the pathophysiological mechanisms underlying the hearing dysfunction. Profound deafness results from an impaired multivesicular glutamate release with abnormal auditory nerve fiber activation and a consequent impairment of spike generation, whereas disordered nerve synchrony underlies the impairment of speech perception in patients showing a stable phenotype of mild hearing loss, consistently with selective impairment of vesicle replenishment at the ribbon synapses with relative preservation of synaptic exocytosis. In addition, our findings indicate that OAEs are preserved much longer than expected in patients showing *OTOF*-related hearing impairment.

S16 L1 - Combinatorial Protection of Cochlear Hair Cells: Not Too Little, But Not Too Much

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Background:
A number of strategies have been proposed to prevent the loss of hair cells, based on cellular processes that can mediate or reduce cellular damage. This includes treatment with survival-promoting growth factors, antioxidants, and inhibitors of apoptosis, autophagy, death pathways, or proteinases. Individual treatments targeting these pathways have been demonstrated to reduce hair cell damage in animal and/or in vitro models. However, the translation to humans has often been disappointing. One reason for this may be the complexity of intracellular damage processes, which includes many parallel and interacting pathways. We hypothesized that manipulating only one aspect of cell damage would be insufficient to produce maximal hair cell protection, but that combined treatments would be more effective.

Methods:
Using data from several screens of compounds targeting different aspects of hair cell damage, we identified inhibitors targeting five different cell damage pathways, and one survival-promoting growth factor. Each were each effective in protecting against hair cell loss in experimental studies. We then tested all 64 possible combinations of these factors to identify an optimal formulation, using dosages below those required individually for hair cell protection.

Results:
Increasing protection was observed for combinations of compounds that consisted of two to four factors, all though not all combinations were equally protective. The optimal combination of four compounds consisted of an anti-oxidant, an apoptosis inhibitor, an autophagy inhibitor and a growth factor. Increasing the number of factors to five or six resulted in decreased protection.

Discussion:
The results support the hypothesis that targeting multiple cellular damage or survival pathways provides more effective hair cell protection. However, they also indicate that blocking too many processes impairs functions that are critical to hair cell survival, resulting in decreased protection.

S16 L2 - Disease-modifying therapy for autosomal dominant hereditary hearing loss in DFNA9

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Globally, hearing loss ranks as the 4th leading cause of disability. Currently, over 1.5 billion people suffer from hearing loss. Sensorineural hearing loss (SNHL) is the most common type and occurs due to pathology of the cochlea, auditory nerve, or central nervous system. Several prospective studies have demonstrated a significant correlation between hearing loss on one hand and age-related cognitive decline and incident dementia on the other hand, which emphasizes the need for a cure for hearing loss. Currently, there are no therapies to halt or prevent the development and progression of SNHL. Though SNHL is manageable with properly fitted hearing aids or cochlear implants (CI), the goal to reach normal speech understanding again cannot be reached. Often this will lead to unsatisfactory outcome for hearing-impaired persons or non-use in case of hearing aids.
SNHL has different known causes which include age, noise trauma, head trauma, ototoxic drugs, and genetic defects. One of those genetic defects is called deafness autosomal dominant 9 (DFNA9), which is a non-syndromic autosomal dominant hereditary disorder. DFNA9 is the most frequent hereditary disorder in Belgium and the Netherlands causing hearing loss at 20-30 years and evolving towards deafness by 60-70 years. Additionally, patients suffer from bilateral vestibulopathy by the age of 40 years. DFNA9 can be the result of several pathogenic variants in the *COCH* gene which encodes the cochlin protein. Previous research has found that cochlin is highly expressed in inner ear structures, incl. the spiral limbus. Mutant cochlin causes diffuse degeneration of those structures as well as hair cell loss.
Ideally, a disease-modifying therapy would have the ability to delay or stop the progression of hearing loss in DFNA9. In DFNA9, only one of the two copies of the *COCH* gene (one inherited from either parent), is mutated and encodes for a toxic protein that affects the aging inner ear in general, and the spiral ligament and spiral limbus more specifically. It therefore presents us with a target anatomically as well as genomically. The DFNA9 population is particularly relevant to develop and evaluate a disease-modifying gene therapy for SNHL because: potential carriers are aware of their hearing-impaired relatives, potential carriers can get routine genetic testing and know their carrier status, once aware of their carrier status, a significant pre-symptomatic stage of several years starts, carriers are aware they will inevitably develop severe-to-profound SNHL and are open to future clinical trials with gene therapy, as identified during a patient advocacy meeting.
Progress will be reported with respect to the generation and phenotyping of a genetically humanized DFNA9 mouse model (p.Pro51Ser variant) and the different strategies to target the mutant *COCH* allele and transcripts.

S16 L3 - An AAV-based antioxidative gene therapy to prevent and treat noise-induced hearing loss

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Background:
Hearing loss affects nearly half a billion people worldwide, with the leading cause in young and aging adults being noise exposure through occupation, recreation, and exposure to ototoxic substances. For noise-induced sensorineural hearing loss (SNHL), the mechanism of action involves the creation of reactive oxygen species molecules that leads to oxidative damage to the hair cells that send auditory information to the brain. When enough damage has accumulated these cells die. Currently there are no FDA approved drugs or therapies to prevent or treat noise-induced sensorineural hearing loss. Therefore, we have developed an adeno-associated virus (AAV) gene therapy that protects these cells from oxidative damage and death. The therapy is based on the CORE HYPOTHESIS that increasing the bioavailability of the antioxidative superoxide dismutase in the cochlear hair cells will prevent oxidative damage associated with noise exposure.

Methods:
Animals received baseline auditory brainstem response recordings followed by intra-cisterna magna injections of either saline or our AAV gene therapy. After three weeks of transgene expression animals were exposed to damaging levels of noise (110 dB SPL) for 2 hours a day over 5 days. Post exposure ABRs were recorded for weeks to track the progression of hearing loss.

Results:
Animals that received the SOD gene therapy showed significant protection from noise-induced hearing loss compared to the control group that developed moderate to severe hearing loss. When used as a treatment following noise exposure, gene therapy animals showed significant reduction in total hearing loss compared to the control group.

Conclusions:
These pilot data provide feasibility and proof of principle data that supports our core hypothesis. Continued work will focus on treatment aspects after noise exposure and prophylactic combination with ear protection.

S16 L4 - Elucidation of Inner Ear Development Mechanisms from Single-cell Genomic Data

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Sensorineural hearing loss (SNHL), caused mainly by cochlear sensory epithelial impairment, is intractable because hair cells within the postnatal mammalian cochlea never regenerate in a physiological situation. However, the treatment of SNHL has become essential due to the correlation between hearing loss and cognitive problems and population aging worldwide.
There are several possible treatment strategies for SNHL. One is the implantation of stem cells induced into cochlear sensory epithelia, which may replace injured cochlear hair and supporting cells. The other strategy is inducing sensory epithelia within the matured inner ear by reproducing its development. Either approach requires precise knowledge regarding inner ear development mechanisms.
Comprehensive gene expression analysis is suitable for elucidating inner ear development. However, its bulk analysis gives rise to limited information because the inner ear comprises multiple sensory epithelia where adjacent cells are differentially matured. In contrast, the single-cell level (scRNA-seq) analysis gives us more information.
We performed the re-analysis of public scRNA-seq data from whole embryonic mice epithelia. Among data from two million single cells of mice embryos, we picked up data from 5000 cells annotated as otic epithelial cells. We classified these 5000 cells into 15 clusters based on known markers of sub-population of inner ear epithelial cells. Using these data, we identified several genes highly expressed in all inner ear sensory epithelia (cochlear, macular, and crista ampullaris epithelia). One of them is early B cell factor 1 (Ebf1). We elucidated the functions of Ebf1 in the inner ear development using Ebf1 deficient mice. Our finding is that Ebf1 limits the proliferation of a prosensory region of the cochlea to develop the proper number of cochlear hair and supporting cells, contributes to the formation of scala tympani and spiral limbus, and, as a result, develops a normal hearing function.

S16 L5 - Auditory neuropathy and related phenotypes associated with m.7471dup variant in MT-TS1

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Recent progress in genetic medicine enabled more precise and personal care for the patients with genetic disorders. The m.7471dup variant in mitochondrial-tRNA Ser (UCN) (MT-TS1) has been known as a genetic cause of sensorineural hearing loss and/or neurological abnormalities. However, detailed auditory features and appropriate clinical interventions for the variant have not been elucidated. Thus, the present study was conducted to reveal genetic features and phenotypic variations of the variant. We investigated eight Japanese families with sensorineural hearing loss associated with the variant. Two families presented with auditory neuropathy, and two other families presented with the phenotype analogous to auditory neuropathy, i.e., auditory brainstem response thresholds much higher than those expected from pure-tone audiometry results. The penetrance of sensorineural hearing loss was 62.5% overall, with 100% penetrance in cases with homoplasmy and 33.3% penetrance in cases with heteroplasmy. The onset of hearing loss was congenital or ≤ 6 years in 80% of the patients. The severity of hearing loss ranged from normal to profound, and four subjects presented with neurological or psychological abnormalities. About 80% of subjects who had newborn hearing screening passed the screening, suggesting late-onset or progressive hearing loss. These findings indicate the importance to provide rigorous follow-up, genetic counseling, and special consideration for educational environment in patients carrying the m.7471dup variant.

S17 L1 - Management of the Unknown Head and Neck Primary in the Era of TORS

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The incentives of identifying a primary head and neck tumour in the initially unknown primary situation are clear: It ameliorates the understanding of the disease by the patient and its overall survival, where the clinician has a clear treatment target and toxicity is potentially minimized in terms of saliva function, swallowing and possibly carotid artery atherosclerosis.
Detection rate in carcinoma of unknown primary (CUP) has improved from 40 to >70% by performing tongue base mucosectomy (TBM) in addition to endoscopy under anesthesia (EUA) with palatine tonsillectomy (PTE) and random biopsies (even with additional methods, such as NBI). TBM thus has an impressive identification rate after negative imaging work up which might be further improved with standardized protocols. Identification of an ipsilateral base of tongue (BOT) tumour leads to precise and unilateral radiation which in turn leads to less long term dysphagia.
In case of an HR-HPV primary tumour, reduction of the radiation field or dose de-escalation is suggested both for primary as well as for adjuvant treatment, pending the outcome of current prospective de-escalation trials.
In the event of complete resection of the primary tumour or when TBM and PTE fail to identify a primary in case of p16-positive nodal disease, radiation of the oropharynx can be omitted with the disease in the neck treated either by surgery alone (single node without extracapsular extension (ECE)) or radiation. In case of multiple positive nodes primary radiation with/without chemotherapy is advised in current guidelines but the addition of chemotherapy for ECE for p16- positive cases is a debated issue.
A negative TBM and PTE with p16- and EBER- negative nodes indicates intensity-modulated radiotherapy (IMRT) of the pharyngo-laryngeal axis.
National guidelines support these strategies without specifying whether TBM should be performed bilaterally (which is advised for PTE). Recent reports of identification rates of over 10 percent in the contralateral BOT support performing bilateral TBM. Postoperative pain and hemorrhage (Clavien Dindo grade II-III) are the most reported complications. TBM performed synchronously with PTE can cause significant additional discomfort for the patient that has led some to perform TBM only after a negative EUA and PTE.
References: 1.Golusinski P, Di Maio P, Pehlivan B, Colley S, Nankivell P, Kong A, Hartley A, Mehanna H. Evidence for the approach to the diagnostic evaluation of squamous cell carcinoma occult primary tumors of the head and neck. Oral Oncol. 2019 Jan;88:145-152. doi: 10.1016/j.oraloncology.2018.11.020. Epub 2018 Nov 30. PMID: 30616785.

S17 L2 - A quantitative approach reveals a different look at distant metastasis

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Objectives:
Emerging evidence suggests that patients with a limited number of distant metastases in head and neck squamous cell carcinomas (HNSCC) have better survival outcomes than those with more extensive metastasis. This concept, referred to as oligometastasis, is still not well-defined. Through this study, we aim to derive the threshold value for the number of metastases and number of affected locations defining oligometastatic disease in HNSCC.

Materials and Methods:
A retrospective cohort study was conducted at the Erasmus University Medical Center, Rotterdam, the Netherlands, including all patients diagnosed with distant metastases between 2006 and 2021. For each patient, the number of distant metastases and affected locations were recorded based on available imaging at the time of diagnosis. Determination of threshold values was performed through Cox regression analyses and a machine-learned K-means algorithm.

Results:
A total of 539 patients with distant metastases were identified, of which 384 patients were untreated for their metastatic foci and included for analyses. The majority of patients (n = 207, 53.9%) had metastasis to one anatomical location, followed by metastases in two anatomical locations (n = 62, 16.1%). The majority of patients had ≥9 metastatic foci (n = 174, 45.3%), followed by one focus (n = 74, 19.3%) and two foci (n = 32, 8.3%). Cox regression analysis and machine-learned K-means models revealed that the number of metastases was not a significant predictor of survival. However, the number of affected locations was a significant predictor of survival, with a threshold value of 2 locations ($p < 0.001$).

Conclusion:
Contrary to the prevalent dogma, the definition of oligometastasis should not be defined by the number of metastases, but rather the number of affected locations. When the cut-off value for oligometastasis in HNSCC is set at 2 affected locations, patients with less locations exhibit a significantly better survival than those with more affected locations.

***S17 L3* - Towards organ preservation via immunotherapy in patients normally undergoing extensive curative surgery and radiotherapy**

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Advanced stage cutaneous SCC (CSCC) is frequently seen in frail elderly patients and often requires extensive surgical treatment with or without adjuvant radiotherapy. The MATISSE trial (NCT04620200) was designed to improve clinical outcome in these patients and to investigate immune cell dynamics early upon neoadjuvant nivolumab (NIVO) and nivolumab plus ipilimumab (NIVO/IPI). 50 patients were randomized for either ARM A: nivolumab (NIVO, 3 mg/kg, weeks 0&2) or ARM B: a combination of NIVO (weeks 0 & 2) and ipilimumab (IPI, 1mg/kg, week 0 only) prior to surgery (week 4). The primary objective was histopathological response rate after neo-adjuvant immunotherapy, defined as the proportion of remaining viable tumor cells in the surgical resection specimen. Median follow-up (FU) at data cut-off was 18 months. Pathological response rates upon neoadjuvant NIVO and NIVO/IPI were 55% and 80%, respectively, accompanied by excellent disease-specific survival (100 %). Grade 3 immune-related-toxicity was observed in 12% (NIVO) and 8% (NIVO/IPI). Ten MATISSE patients withdrew consent to surgery, of whom 1 patient with progressive yet operable disease. The other 9 patients reached a clinical complete remission (CCR) and were free from disease at median 24 months FU. This observation raises the crucial question whether standard of care, i.e. surgery with or without adjuvant RT, is still a prerequisite for cure in early responders.

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S17 L4 - Discrete prognostic implication of sarcopenia according to nutritional status in surgically treated patients with hypopharyngeal cancer

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Background:
Nutritional status and sarcopenia affects the prognosis of head and neck cancers including hypopharyngeal cancer. Hypopharyngeal cancer patients tend to exhibit sarcopenia, which is associated with poor treatment outcomes. This study aims to determine the correlation between nutritional status and sarcopenia, and their prognostic role in surgically treated hypopharyngeal cancer.

Materials and Methods:
Patients who had been diagnosed with squamous cell carcinoma originating from the hypopharynx and underwent surgery between January 2009 and December 2019 were enrolled in this study. The median neutrophil-to-lymphocyte ratio and prognostic nutritional index (PNI) of the cohort were considered the cut-off values. Sarcopenia was evaluated by measuring skeletal muscle index (SMI) at the third lumbar vertebra. Clinical and serological factors predictive of survival outcomes were evaluated.

Results:
Patients with high PNI showed better 5-year overall survival (52.8% versus 27.2%, p=0.001) and disease-free survival (59.6% versus 44.6%, p=0.033) than those with low PNI. Likewise, patients with low SMI showed worse 5-year overall survival (25.0% versus 60.9%, p=0.002) and disease-free survival (42.4% versus 68.7%, p=0.034) than patients with high SMI. Among the patients with high PNI, those with sarcopenia displayed significantly worse overall survival than those with high SMI (78.0% versus 34.4%, p=0.049). High PNI with high SMI (presented better overall (p = 0.010) and disease-free survival (p = 0.055) than any other group.

Conclusions:
Both sarcopenia and PNI were associated with the prognosis of hypopharyngeal cancer. Considering that PNI and sarcopenia indicate the nutritional status, nutritional status may be a significant risk factor. Therefore, nutritional support that ameliorates sarcopenia may improve survival outcomes in surgically treated patients with hypopharyngeal cancer.

S17 L5 - Prognostic significance of metabolic tumor volume in patients with recurrent and/or metastatic head and neck squamous cell carcinoma

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Background:
The standard therapy for recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) is systemic therapy with immune checkpoint inhibitors (ICIs) or platinum-based chemotherapy. We aimed to determine whether metabolic tumor volume (MTV), determined using 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET), can predict treatment outcomes for patients with R/M HNSCC.

Method:
We performed a multicenter retrospective chart review of patients treated with either ICIs or platinum-based chemotherapy as the first-line therapy for R/M HNSCC. The overall survival rate was estimated using the Kaplan–Meier method and tested using a log-rank test. Hazard ratios (HRs) for overall survival were calculated using the Cox proportional hazards model. The cut-off value for MTV was determined using time-dependent receiver operating characteristic curve analysis.

Results:
We included 114 patients treated with platinum-based chemotherapy and 56 treated with ICIs. The median survival time of the chemotherapy cohort was 12.8 months. Median survival time for low and high MTV groups were 19.8 months and 10.8 months, respectively ($p < 0.001$). Cox proportional hazards analysis revealed that p16 status and total MTV were independent prognostic factors for overall survival. In the ICI cohort, the median survival time was 21.1 months. The median survival time was not reached in the low MTV group and 19.3 months in the high MTV group ($p = 0.112$). Cox proportional hazards analysis revealed total MTV and combined positive score as independent prognostic factors for overall survival.

Conclusion:
MTV was an independent prognostic factor for both the chemotherapy and ICI cohorts. MTV can be used for risk stratification of R/M HNSCC.

S17 L6 - Transoral videolaryngoscopic surgery (TOVS) for elderly patients with laryngopharyngeal cancer

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Introduction: Japan's aging population is increasing rapidly, with the proportion of those aged ≥65 years reaching 28.9% in 2021. Simultaneously, the incidence of head and neck cancers in older patients is increasing. In 2004, we developed transoral videolaryngoscopic surgery (TOVS) as a minimally invasive, non-robotic, endoscopic surgery for localized early stage laryngopharyngeal cancer. Over 200 patients have undergone this procedure at our institution, with favorable outcomes reported. However, the efficacy, safety, and indications of TOVS in older patients remain unclear. This study evaluated the treatment outcomes and risks of long-term hospitalization for TOVS in older patients, especially those aged ≥75 years.
Material and Methods: This case series included patients who underwent TOVS for supraglottic or hypopharyngeal cancer at our institution between April 2010 and May 2021, with a follow-up of >2 years after surgery. Patients were divided into older (age ≥75 years) and control groups (age <75 years). Treatment outcomes included 5-year overall survival (OS), disease-specific survival (DSS), local control rate (LCR), and larynx preservation rate (LPR). Postoperative complications, tracheotomy status, enteral nutrition, and swallowing function were also assessed.
Results: In total, 110 patients underwent TOVS (33 older, mean [SD] age 79.1 [3.2] years; 77 control, mean [SD] age 63.8 [7.7] years). No significant differences were observed in the 5-year OS, DSS, LCR, and LPR between the older and control groups (89.5% vs. 92.4%, 100% vs. 91.7%, 97.0% vs. 86.7%, and 100% vs. 98.7%, respectively). Postoperative complications were similar between groups. In the older group, G8 score ≤14, extensive resection, and arytenoid resection significantly delayed soft diet initiation by ≥14 days postoperatively. For all patients, pT classification, arytenoid resection, extensive resection, radiation therapy, and tracheotomy were also significantly associated with delayed soft diet initiation by ≥14 days postoperatively. Six months postoperatively, four older patients had swallowing dysfunction of stage III or higher on the Functional Outcome Swallowing Scale. All four patients had multiple factors that were significantly associated with the time to initiate soft diet intake (≥14 days postoperatively).
Conclusions: TOVS is a safe and effective treatment for supraglottic and hypopharyngeal cancer in older patients. Patients without a history of radiation therapy, tracheotomy, arytenoid resection, or extensive resection and with a G8 score of ≥15 can avoid long-term hospitalization due to postoperative swallowing dysfunction.

S18 L1 - Streptococcus angionosus group, much more than commensals

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Background:
The Streptococcus Angionosus Group (SAG) are human commensals in the upper respiratory tract. SAG has also been recognized having pathogenic potential. We conducted a study of severe SAG infections in the head and neck area to broaden the understanding of clinical presentation, disease course and treatment.

Methods:
A retrospective medical record study was performed of patients with SAG-infections in the head and neck area during 2019-2023 at Skåne University Hospital. Patient characteristics, infection site, disease course, treatment and microbiology were examined.

Results:
Of 61 patients, median age was 41 years, 59% were male. In total 93% had surgical intervention, 75% were hospitalized and 18% needed ICU-care. Median initial c-reactive protein (CRP) was 155mg/L. Higher CRP-value raised the probability of ICU-care increased (p-value=0.0015). All 61 patients were treated with antibiotics (80% with intravenous antibiotics). In 69% there was abscess formation and 64% had polymicrobial growth. Common infections were sinusitis (31%), inflammation and abscess in the mouth region (23%), retropharyngeal or parapharyngeal abscess (21%), peritonsillitis (15%) and orbital infections (10%). Sinusitis and orbital infection were most common among children 0-17 years (p-value<0.05) while inflammation and abscess in the mouth region only occurred among adults. All cases with retropharyngeal or parapharyngeal abscess except one occurred in adults.

Conclusion:
SAG is indeed pathogens with the ability to cause severe infections in the head and neck area. This study emphasizes the importance of surgical treatment in combination with antibiotics to treat severe SAG-infections in the head and neck area. Initial CRP-value seems to predict the severity of disease course. SAG is commonly seen in abscesses and this study proposes sinusitis and orbital infections with SAG being most prevalent among children while inflammation and abscess in the mouth region and retropharyngeal or parapharyngeal abscess are more common among adults.

S18 L2 - Head and neck cancer treatment based on medical-dental collaboration

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Background: head and neck cancer treatment should generally be led by otorhinolaryngology–head and neck surgeons, oral cancer treatment is also performed in dentistry in Japan. In spite of the inappropriate situation in which medicine and dentistry can compete with each other, our university hospital has been practicing head and neck cancer treatment with an emphasis on medical-dental collaboration.

Materials and Methods: Okayama University Hospital Head and Neck Cancer Center was established in 2012 as the first national university to focus on medical-dental collaboration. Since then, the medical and dental departments, nursing department, pharmaceutical department, rehabilitation department, patient support center, and perioperative management center have cooperated to provide consistent team care. We reviewed treatment results to date. In addition, to clarify the current status of oral cancer treatment in Japan, the national database was used to identify the number as well as the composition by gender, age group and prefectural differences of medical and dental surgeries in Japan. The percentage of oral cancer cases treated by head and neck surgeon at facilities specializing in head and neck cancer was also surveyed.

Results: All head and neck cancer cases in our university hospital, not limited to oral cancer, are consulted to dentistry and an individualized oral care plan is developed. All cases are then started on preventive dental care, followed by conservative and prosthetic dental treatment as needed. Maxillary and mandibular reconstruction is being performed taking advantage of good medical-dental collaboration. Regarding the current situation in Japan, although the total number of oral surgeries was almost equal between medical and dental departments, a larger proportion of surgeries for early-stage cases (e.g., partial resection) were performed by dental departments. Most surgeries for advanced cancer (e.g., subtotal resection) were performed by medical departments. There were also large differences between prefectures, which was thought to reflect the presence of dental schools and healthcare access status.

Discussion and Conclusions: In order to provide the best possible medical care to head and neck cancer patients, the strengths of the medical and dental departments must be utilized in a coordinated manner. We believe that appropriate information sharing and discussion after the patient's visit to our hospital is necessary.

S18 L3 - Possible Mechanism of Carcinogenesis of Temporal Bone Squamous Cell Carcinoma

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Etiologic factors in squamous cell carcinoma of the temporal bone (TBSCC) have been proposed, such as exposure of ultraviolet (UV) light, chronic ear inflammation, or chemicals. We investigated the mechanism of malignant transformation of TBSCC from the genetic and epigenetic aspects. Whole exome sequencing was performed on surgical specimens from 11 primary tumors. The most frequently mutated gene was TP53, followed by CDKN2A, NOTCH1 and so on. Loss-of-function mutation of tumor suppressor genes was predominant, and the pattern of mutation was the most similar to that of head & neck squamous cell carcinoma (HNSCC). APOBEC-associated mutation was the most common mutational signature, being neither smoking-related signature like some of HNSCC nor UV-related signature like skin cancer. It indicated that inflammation-induced mutagenesis could be a main cause of TBSCC carcinogenesis. Wound formation induces tissue repair by transcriptional reprogramming through epithelial-mesenchymal transition (EMT) process. TP53 and Notch signal regulate tissue repairing program. EMT was also reported to be poor prognostic factor in TBSCC. The prognosis of TBSCC has been reported to be dependent on the invasive properties in TBSCC. We previously showed that conditional activation of transcriptional co-activator Yes-associated protein 1 (YAP1) rapidly raises SCC in mice tongue. We focused on YAP1-induced transcription or "transcriptional reprogramming" in TBSCC. High expression of YAP-1 activator, laminin5-ɤ2 and emmprin-CD73-CAF, were poor prognostic factors in TBSCC. These results indicated that YAP1 plays a certain role for the invasive property of TBSCC. YAP1 is reported to be one of important inducers to form super-enhancer (SE) region to produce abundant transcript. We did the functional analysis related to YAP1-induced transcription by ChiP and RNA sequencing in primary TBSCC. 8 out of 15 p-EMT genes were highly expressed. YAP1 activation and p-EMT related gene expression showed significant correlation in the cancer genome atlas (TCGA) program HNSCC. SE region where YAP1 binds to were rich in binding motif for PITX2 transcript factor and high expressed PITX2 showed poor prognosis in TBSCC. Transcriptional target of SE was HIF1A which induced p-EMT genes by the use of TBSCC primary tumor. HIF1A expression was elevated in TBSCC. Our data suggested that YAP1/PITX2-induced transcriptional machineries could be a potential prognostic biomarker of TBSCC patients.

S18 L4 - Whiteish color change around the FAF in otosclerosis

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Background:
In otosclerosis, in addition to the reduced mobility of the stapes, dilated blood vessels on the promontory, as well as a low-density area around the fissure ante fenestrae (FAF) on HRCT, can be observed. Since we started endoscopic stapes surgery, we have also noticed a whiteish color change (WCC) of the bone surface around the FAF, and we investigated the significance of this surgical finding.

Materials and Methods:
We retrospectively reviewed surgical videos of 27 cases of otosclerosis and 28 cases of conductive hearing loss due to pathologies other than otosclerosis (controls), both of which were operated on endoscopically at the University of Tokyo Hospital, and the presence or absence of WCC was examined. In otosclerosis, the presence or absence of WCC was compared with the preoperative hearing level, preoperative air-bone gap, and low-density area on HRCT.

Results:
WCC was present in 11 (41%) of 27 cases of otosclerosis but none in 28 control cases. The mean preoperative hearing thresholds and air-bone gaps were 57.5 dB and 40.0 dB, respectively, in 11 otosclerosis cases with WCC and 63.7 dB and 32.2 dB in 16 otosclerosis cases without WCC. The low-density area around the FAF on HRCT was present in 9 of 11 otosclerosis cases with WCC and 9 of 16 otosclerosis cases without WCC, with no statistically significant differences.

Conclusions:
Although there was no correlation between WCC around the FAF and preoperative hearing level and air-bone gap or HRCT finding, the WCC is a unique finding in otosclerosis and therefore is considered supportive of obtaining accurate diagnosis during surgery.

S18 L5 - Appropriate Ossicle Palpation during Otologic Surgery: Variations in Judgments and How Surgeons Exert a Large Force on the Ossicles

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Objectives: To confirm the ossicular fixation, their mobility is examined using a needle. We examined 1) whether palpation to assess ossicular mobility causes the exertion of significant pressure on the inner ear, and 2) whether the perception of ossicular mobility measured by multiple surgeons was similar.

Study design: Surgical skills testing

Setting: Doctors from multi centers study

Methods: 1) The doctors were instructed to palpate the probe attached to the needle approximately three times with the same degree of force as in normal palpation. The force applied to the spring was measured and the variation in the measured values was examined. 2) Which degree of fixation may a otologic surgeon determine to require reconstruction of the ossicles?

Results: 1) The measurements showed significant variability among surgeons. The less the force of the “palpation” of ossicles, the less the vibration transmitted to the inner ear.
2) The surgeons were asked to palpate springs of varying stiffness and identify the stiffness of the springs that were comparable to the ossicular fixation that necessitates ossiculoplasty. The Only six of 21 surgeons could correctly determine the stiffness. There was no correlation between accurate perceptions of the ossicle stiffness and the application of strong pressure to the ossicles.

Conclusion: Quantitative and objective measurements revealed a wide variation between surgeons, even after a single round of palpation of the ossicles. It was more difficult than expected to palpate the ossicles without applying a significant force to the inner ear to determine whether reconstruction was necessary.

S18 L6 - Assessment and management of postoperative pain in pediatric otolaryngology

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Pain is one of hospital patients' most common complaints and is the main reason they seek medical help. Pain is always subjective, so its severity should be assessed individually for each patient. The main issue with pain management in children is the difficulty involved in evaluating it. Numerous studies have developed tools that would accurately assess pain intensity in children in the postoperative period. Adequate postoperative pain assessment in pediatric patients may significantly improve their comfort and quality of life. Postoperative pain prolongs recovery and hospitalization; therefore, the severity of the pain should be part of a routine assessment. The child's age, language, ethnicity, and cognitive ability should be considered whenever a tool is applied to measure pain. There is no universal method for pain assessment that is appropriate for every pediatric patient. We present the subjective methods of postoperative pain assessment, including new objective diagnostic procedures and the latest guidelines for postoperative pain therapy in pediatric patients.

S18 L7 - Direct Microneedle Intracochlear Injection of Gadodiamide through the Round Window Membrane Enables Rapid Intracochlear Imaging on MRI

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Funding Sources:
Funding for this project was provided by the Columbia University Medical Center's Irving Institute Imaging Pilot Grant and Department of Defense CDMRP W81XWH2210983.

Objectives: Magnetic resonance imaging (MRI) has been proposed as a method for inner ear imaging and diagnosis of endolymphatic hydrops–a hallmark of Menière's disease. However, its potential is largely limited by the prolonged time required for contrast to reach cochlear turns following intravenous (IV) or intratympanic (IT) delivery, the high contrast dosage needed, and the inconsistent perilymph signal intensity enhancements among patients. In this study, we aim to address these limitations by investigating the utility of microneedle-mediated intracochlear (IC) injection of gadodiamide to achieve consistent and efficient contrast delivery with minimum contrast dosage.

Materials and Methods: Following surgical exposure, a 100 µm diameter microneedle with 35 µm lumen was advanced to perforate the guinea pig round window membrane and 1 µL of gadodiamide diluted in artificial perilymph to a concentration of 17.4 mM was injected into the cochlea. Serial MRI imaging was performed in a post-mortem animal using a 9.4 tesla small-animal MRI. Maximum intensity projections of MRI scans were generated with 3D Slicer to visualize diffusion of contrast from basal to apical turns over time; mean intensities in defined regions of interest (ROIs) were calculated. Contrast diffusion time and intensity enhancements were determined.

Results: Contrast reached the first two and half turns of both the scala tympani (ST) and scala vestibuli (SV) within 60 minutes. By 90 minutes post-injection, contrast penetrated apical turns of both ST and SV. Intensity enhancements calculated at 90 minutes post-injection demonstrated intensity enhancements exceeding 100% in the first turn of both ST and SV, as well as the first half of the second turn of ST.

Although intensity enhancements in the third and apical turns were lower, they still ranged from 12% to 38%.

Conclusions: Direct injection of gadodiamide into the cochlea enables controllable and efficient contrast delivery utilizing a total contrast dosage orders of magnitude smaller compared to IV and IT administration. Additionally, our previous studies have shown no hearing loss and complete round window membrane healing following *in vivo* microneedle IC injection, thus, making IC injection a viable alternative to commonly used IV and IT injections to enhance the feasibility of contrast-enhanced cochlear MRI for diagnosing endolymphatic hydrops.

S19 L1 - Transmastoid superior semicircular canal dehiscence plugging: VHIT findings

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Background: Superior semicircular canal dehiscence (SSCCD) syndrome is a clinical condition characterized by a combination of vestibular and audiological symptoms resulting from the dehiscence of the superior semicircular canal (SSCC). Surgical intervention has proven effective in managing SSCCD syndrome, particularly for patients experiencing debilitating symptoms. The initially described surgical approach commonly involved middle fossa craniotomy with resurfacing. However, an alternative technique involves a transmastoid approach, which directly addresses the SSCC by plugging it. The video head impulse test (VHIT) enables quantitative assessment of canal function through the analysis of angular vestibulo-ocular reflexes (aVOR). Consequently, postoperative evaluation of this reflex could verify the efficacy of SSCC plugging via the transmastoid approach. The primary objective of this study was to evaluate VHIT results following SSCC plugging using the transmastoid approach.

Materials and Methods: This study included patients diagnosed with superior semicircular canal dehiscence (SSCCD) syndrome experiencing debilitating symptoms who underwent SSCC plugging via a transmastoid approach. Through retrospective chart and literature reviews, postoperative VHIT findings, pre- and postoperative audiological/vestibular symptoms, and audiograms were analyzed at a tertiary care university hospital.

Results: Patients who underwent SSCC plugging via the transmastoid approach demonstrated a significant postoperative VHIT deficit in SSCC function (range 0.34-0.70, median gain function 0.41, mean gain function 0.46, standard deviation 0.15, p = 0.0391). Nearly all patients experienced improvements in their preoperative symptoms, and no surgical complications were observed. The literature review further confirmed the safety and effectiveness of this surgical technique.

Discussion and Conclusion: Postoperative VHIT can effectively assess the efficacy of the transmastoid approach by indicating an intentional deficit in SSCC function, thus confirming successful SSCC plugging. Long-term VHIT monitoring of these patients would be valuable in determining whether these deficits persist and if any recovery of function correlates with the recurrence of debilitating symptoms. Overall, this series demonstrates the feasibility, safety, and effectiveness of SSCC plugging via the transmastoid approach in all patients.

S19 L2 - What is the most important factor to preserve hearing in lateral semicircular canal fistula surgeries, fistula size or bony structure?

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Purpose:
Cholesteatoma on lateral semicircular canal (LSCC) fistula > 2 mm in size is likely to be unmanipulated due to the risk of sensorineural hearing loss. However, the matrix can be successfully removed without hearing loss when it is > 2 mm. The purpose of the study was to evaluate surgical experience over the past 10 years and to suggest the important factor forthe hearing preservation in LSCC fistula surgeries.

Methods:
According to the fistula size and symptoms, 63 patients with LSCC fistula were grouped as follows: Type I (fistula <2 mm), Type II (≥ 2 mm and < 4 mm without vertigo), Type III (≥ 2 mm and <4 mm with vertigo), Type IV (≥ 4 mm), and Type V (any size fistula but with deafness at the initial visit). The cholesteatoma matrix was meticulously manipulated and removed by experienced surgeons.

Results:
Only two patients completely lost their hearing after surgery (4.5%). However, the loss was inevitable because their cholesteatomas were highly invasive and there was also facial nerve canal involvement; thus, the bony structure of the LSCC was already destroyed by the cholesteatoma. Unlike these two Type IV patients, Type I–III patients, and those with a fistula size < 4 mm, did not lose their sensorineural hearing. If the structure of the LSCC was maintained, hearing loss did not occur even if the fistula size ≥ 4 mm.

Conclusions:
The preservation of the labyrinthine structure is more important than the defect size of the LSCC fistula. If the structure is intact, cholesteatoma matrices lying on the defect can be safely removed, even though the size of bony defect is large.

S19 L3 - How can we distinguish angiopathic sudden sensorineural hearing loss from the others?

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Idiopathic sudden sensorineural hearing loss (ISSNHL), sometimes accompanied by vertigo, is considered an otologic emergency. When it doesn't recover, the remaining hearing loss seriously affects the quality of life. ISSNHL is caused by a variety of inner ear pathologies, the etiology and pathogenesis of which remain unknown. Some reports suggest that viral infections, autoimmunity, and vascular impairments contribute to the underlying pathogenesis of ISSNHL.

We focused on the ISSNHL due to vascular impairment which could be called angiopathic sudden sensorineural hearing loss (ASSNHL) or angiopathic sudden deafness (ASD). Previously we reported that atherosclerosis-related factors are a risk for severe ISSNHL and that daily anticoagulant medication is a poor prognostic factor for ISSNHL. We believe it is important to establish diagnostic criteria for ASSNHL which could lead to the rapid development of treatments. However, we faced the very important question "How can we distinguish angiopathic sudden sensorineural hearing loss from the others?"

To answer the question, we cast a spotlight on the labyrinthine artery, which supplies blood to the inner ear. The vestibulocochlear artery (VCA) supplies blood flow to the basal turn of the cochlea and posterior semicircular canal (PSC). Anterior and lateral semicircular canals receive the blood supply of the anterior vestibular artery (AVA). We clinically identified the ISSNHL patients with isolated PSC dysfunction (iPSD) which were diagnosed by video head impulse test (vHIT). The patients with iPSD had significantly more comorbidity of coronary artery diseases and daily antithrombotic medications than the other patients. The audiograms of these patients at the initial visit showed profound, flat, or high-frequency descending forms. We consider that iPSD is an indirect finding of impaired blood flow in the VCA, a part of the pathology of ASSNHL.

S19 L4 - Hyperacusis after noise-induced hearing loss: mechanisms, biomarkers, and proof-of-concept treatment

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Exposure to intense noise permanently damages cochlear sensory cells and primary afferent nerve endings. Sound processing centers of the brain compensate by reducing levels of inhibition, thereby sensitizing central neurons to diminished inputs from the damaged ear. Work from our lab and others has shown that this compensatory brain plasticity often overshoots the mark, introducing neural hyperactivity, hypersynchrony, and hyperresponsiveness to spared frequencies. These central neurophysiological changes are assumed to be proximal mediators of tinnitus, loudness hypersensitivity, and sound aversion, though a direct connection has yet to be proven. Here, I will demonstrate a causal link between sensorineural hearing loss, brain plasticity, and perceptual disorders, with a particular emphasis on the perception of loudness and dysfunction in parvalbumin-expressing inhibitory interneurons (PVNs) of the mouse auditory cortex (ACtx). In normal hearing mice, optogenetic inactivation or activation of ACtx PVNs immediately shifted behavioral loudness reporting to hyperacusis or hypoacusis, respectively. Following noise-induced high-frequency hearing loss, inhibition was reduced, ACtx was hyperresponsive, and mice exhibited loudness hyperacusis to frequencies bordering the cochlear lesion. If cortical PVN hypofunction was the direct cause of hyperacusis after hearing loss, we reasoned that activating PVNs in mice with ongoing hearing loss would reverse their hyperacusis. We confirmed this prediction and developed several paradigms for a single, brief bout of PVN activation that reversed hyperacusis for up to one week. This finding is significant because it shows that full reversal of a common auditory perceptual disorder can be achieved (in laboratory animals) by modifying activity in sound processing centers of the brain even when ear damage remains untreated. We have built on our animal studies by developing non-invasive, fast, and low-cost video-based measurements for tinnitus and hyperacusis severity in human subjects. Our ongoing work combines insights from our animal studies on the neuroscience of tinnitus and hyperacusis with these new classes of biomarkers with the ultimate goal of developing new therapies for these disorders.

S19 L5 - Auditory Agnosia Caused by Bilateral Auditory Cortex Lesions due to Herpes Encephalitis of An Infant but Cortical Deafness at Period of Teenager Presenting Profound Hearing Loss with Normal ABR and DPOAE-37 years follow up

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Background: There are two types of central auditory disorders due to pathology of the bilateral auditory cortices in adult patients: auditory agnosia with residual hearing and cortical deafness with total hearing loss. However, long-term hearing changes of auditory agnosia in infants are unknown.
Materials and Methods: A male patient incurred herpes simplex encephalitis at his age of 1 year and 3 months, which caused bilateral auditory cortex lesions resulting in his auditory agnosia with residual hearing. We followed this patient until he was 38 years old. His brain MRI were taken at different ages and his hearing abilities were repetitively evaluated by VRA, pure tone audiometry, ABRs and DPOAE.
Results: He was made a diagnosis of auditory agnosia caused by bilateral auditory cortex lesions due to herpes encephalitis. His subjective hearing decreased over time from normal hearing revealed by VRA and pure tone audiometry in childhood. At period of teenager, he developed a profound hearing loss bilaterally manifesting cortical deafness although auditory functions of his peripheral hearing organs and brainstem auditory pathways were well preserved. Before his onset of herpes encephalitis, he could speak several words. Thereafter, he was not able to speak nor comprehend spoken language and was educated at a school for the deaf from kindergarten to high school by visually based communication techniques such as cued speech, finger spelling, sign language, and written language. Upon graduating from high school, he commuted to a day-care facility where work continued to improve his communication using sign language and written conversation.
Discussion and Conclusion: The auditory agnosia in adult patients with bilateral auditory cortex lesions is mainly caused by bilateral cerebrovascular accidents. Bilateral auditory cortex lesions can manifest as auditory agnosia, preservation of some residual hearing, or cortical deafness, a total loss of hearing. In adults, auditory agnosia or cortical deafness is usually caused by two episodes of cerebral infarction. However, in pediatric cases, auditory agnosia is frequently caused by herpes encephalitis. Adult cases have been extensively studied but long-term follow-up studies of pediatric cases have rarely been reported.
In this case report, we studied hearing changes based on our long-term experiences of a male patient who, at a very young age, was diagnosed with auditory agnosia which progressed to cortical deafness at period of teenager.
In conclusion, neuronal degeneration of bilateral medial geniculate body of the patient may have occurred as a result of retrograde degeneration of auditory radiation due to bilateral auditory cortex lesions and manifested cortical deafness.

S19 L6 - Clinical Impact of Hyperbaric Oxygen Therapy Combined with Steroid Treatment for Sudden Sensorineural Hearing Loss: a case-control study

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Objectives:
To evaluate the clinical efficacy of hyperbaric oxygen therapy (HBOT) as a primary therapy combined with standard systemic corticosteroid treatment for sudden sensorineural hearing loss (SSNHL) compared to treatment without the use of HBOT (non-HBOT).

Methods:
298 SSNHL patients were included. Inclusion criteria encompassed first onset and treatment, WHO grade 3 or 4 initial hearing impairment, receipt of systemic corticosteroid therapy within 14 days of symptom onset, and initiation of HBOT within the same timeframe for the case group. The primary outcome measure was the difference in hearing improvement (mean hearing level in decibels, dB) between the two groups.

Results:
The study included 67 patients in the HBOT group and 68 in the non-HBOT group. The HBOT group exhibited significantly greater hearing improvement (adjusted difference: 7.6 dB, 95% CI 0.4-14.7; p = 0.038). Patients without vertigo in the HBOT group demonstrated substantial hearing improvement (11.5 dB, 95% CI 2.3-20.6; p = 0.014), while those with vertigo showed no significant improvement (-1.8 dB, 95% CI -11.8-8.3; p = 0.729). The HBOT group also had a significantly higher association with complete recovery (IPTW-adjusted odds ratio: 2.57, 95% CI 1.13-5.85; p = 0.025).

Conclusion:
In SSNHL, HBOT combination therapy yielded significantly improved hearing outcomes compared to non-HBOT treatment.

S20 L1 - Usher Syndrome - Past, Present and Future

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Usher syndrome (USH) is the most common genetic condition responsible for combined hearing and vision loss. Bilateral vestibular areflexia are also observed in some cases. Around 400.000 are affected world wide.The syndrome was first described by von Graefe in 1858, but later named by Charles Usher, who presented a large number of cases with hearing loss and retinopathy in 1914. The cause of deafblindness is cochlear hair cell loss and retinal photo-receptor loss. USH comprice three main clinical types: 1, 2, and 3, which are caused by mutations in different genes further divided into different subtypes. To date, 11 causative genes have been identified. USH is inherited in an autosomal recessive pattern. Digenic, bi-allelic, and polygenic forms have also been reported, in addition to dominant or nonsyndromic forms of genetic mutations. This speech will describe evolvement of epidemiology, clinical and genetic diagnostics, prognosis, the role of CI, ongoing genetic treatment and future treatment possibilities

S20 L2 - Navigation in temporal bone and lateral skull base surgery

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The temporal bone and lateral skull base are anatomically complex fields with a crowd of critical structures and significant individual variability. Surgical approaches in this area require a deep understanding of the surgical landmarks and a methodical approach to recognize them.
Image-guided surgical navigation (IGSN) has an established track record in surgeries of the anterior skull base, as well as cranial surgery. Registration using facial landmark identification is commonly used during surgery for the anterior skull base, but has been limited in lateral skull base IGSN because of the lack of natural, prominent and stable anatomic landmarks in this area, while use of anterior facial landmarks results in a higher than acceptable registration error. The only alternative involves the use of more invasive registration methods such as fiducially.
Because of these limitations in registration as well as the resultant large error, the use of navigation has been limited in temporal bone surgery.
We hereby present the results of a small cadaveric study using a novel, non-invasive, registration method that results in high accuracy. We also review the current literature on the use of navigation and its appropriate indications in the temporal bone and lateral skull base.

S20 L3 - A multi-omics evaluation of the microbiome in oral cavity squamous cell carcinoma

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Background: The prevalence of Oral Cavity Squamous Cell Carcinoma (OSCC) without traditional risk factors has been increasing in recent years. Here from a cohort of HPV-negative patients we simultaneously profiled the oral mucosal microbiota, host genome-wide transcriptome and DNA CpG methylation to explore the genetic basis of host-microbiota interactions as a potential factor in the development of OSCC
Materials and Methods: This study was approved by The Joint Chinese University of Hong Kong—New Territories East Cluster Clinical Research Ethics Committee (CREC reference numbers 2015.396 and 2017.143). Tumor and AN tissues (≥5 cm away from the margin of the tumor) were collected at the time of surgery. Microbiota 16S rRNA gene V3–V4 amplicon sequencing, HPV genotyping, lncRNA-seq, CpG methylation with bisulfite sequencing were done with bioinformatic analysis.
Results: In this study of 90 patients, the mucosal bacterial community, host genome-wide transcriptome and DNA CpG methylation were simultaneously profiled in tumors and their adjacent normal tissues of OSCC patients. Significant enrichment in the relative abundance of seven bacteria species (*Fusobacterium nucleatum, Treponema medium, Peptostreptococcus stomatis, Gemella morbillorum, Catonella morbi, Peptoanaerobacter yurli and Peptococcus simiae*) were observed in the OSCC tumor microenvironment. These tumor-enriched bacteria formed 254 positive correlations with 206 up-regulated host genes, mainly involving signalling pathways related to cell adhesion, migration and proliferation. Integrative analysis of bacteria-transcriptome and bacteria-methylation correlations identified at least 20 dysregulated host genes with inverted CpG methylation in their promoter regions associated with enrichment of bacterial pathogens, implying a potential of pathogenic bacteria to regulate gene expression, in part, through epigenetic alterations. An *in vitro* model further confirmed that *Fusobacterium nucleatum* might contribute to cellular invasion via crosstalk with the E-cadherin/β-catenin signaling, TNFα/NF-κB pathway and extracellular matrix remodelling by up-regulating SNAI2 gene, a key transcription factor of epithelial-mesenchymal transition.
Discussion and Conclusions: Through a multi-omics approach to explore complex host-microbiota interactions we gained important insights into the genetic and functional basis in OSCC tumorigenesis, which may serve as a precursor for hypothesis-driven study to better understand the causational relationship of pathogenic bacteria in this deadly cancer.

S20 L4 - Repair of spontan cerebrospinal otorrhea using middle fossa approach

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Cerebrospinal fluid (CSF) otorrhea frequently occurs as a result of trauma, surgery, neoplasm, or congenital malformations. Trauma history and meningitis may provide clues for the suspected CSF leakage in patients who report aural fullness, hearing loss, tinnitus, and imbalance. Conversely, spontaneous CSF containing middle ear effusion/otorrhea (MEE/OTO) can occur without temporal bone trauma or any prior meningitis episode. There is an important association between spontaneous CSF otorrhea, obesity, and increased intracranial hypertension in adults. A correct diagnosis can easily be missed, particularly in adult and geriatric patients.
Spontaneous adult-onset CSF otorrhea is often associated with tegmen tympani defects. Defects may be congenital or due to aberrant arachnoid granulations. According to the arachnoid theory, some arachnoid granulations may not find venous terminations and penetrate the dura mater, which results in defects in the bony tegmental plate of the tympani. Otorrhea with tegmen tympani defects can cause hearing loss and predispose to meningitis. Although symptoms of spontaneous CSF otorrhea are rare, autopsy studies showed that single defects of the tegmen tympani were present in 15%-34% of specimens, and multiple defects occurred in less than 1% of them.
Middle ear effusion with conductive hearing loss is the most common presenting symptom in CSF otorrhea. Diagnosis is usually made through ongoing, clear odorless, watery type otorrhea after ventilation tube application or myringotomy in suspected cases. The leakage may vary with various maneuvers that increase intracranial pressure (ICP), such as Valsalva maneuver and jugular vein compression. The diagnosis can be supported by β2-transferrin, glucose, and β-trace protein analysis in the suspected fluid.
Magnetic resonance imaging (MRI) and computed tomography (CT) are used to show the defects, brain tissue, and the meninges.
We presented 12 cases of spontaneous CSF otorrhea with a defect on the tegmental plate of the temporal bone. High-resolution CT (HRCT) scan of the temporal bones showed the tegmen tympani defects. The defects were successfully repaired with temporal muscle fascia or fascia lata graft and fibrin glue using the middle cranial fossa approach via craniotomy.

S20 L5 - Prognostic Factors in Myringoplasty

Nicola Quaranta
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Introduction:
Tympanic membrane perforation (TMP) is the result of recurrent or chronic otitis media, iatrogenic or traumatic events. It may sometimes require a surgical repair, known as myringoplasty, with the purpose of rebuilding a barrier between external and middle ear, and restoring a good hearing level. The aim of this study is to identify the prognostic factors that may affect the outcomes of myringoplasty.

Materials and methods:
A retrospective chart review was carried out by including all patients who had undergone myringoplasty for TMP in our Institution in the period between January 2017 and December 2021. All the potential prognostic factors were evaluated.

Results:
A global success rate of 90.1% was found, with a satisfying hearing recovery in 71.5% of cases. Reperforation was demonstrated to be more frequent in children, in patients with a poor educational level, in the presence of tympanosclerosis and involvement of the anterior quadrants of the membrane.

Conclusions:
Our data show that knowing the prognostic factors may help adapting the techniques and indications to every single case, thus improving the outcomes of myringoplasty.

S20 L6 - Access to the provision of hearing health in patients with presbycusis: A new model of care for public health insurance in Chile

Mariela C. Torrente
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Introduction:
In Chile the government pays for hearing devices in adults over 65 years of age, but the prescription depends on the access to an otorhinolaryngologist specialist, with more than one year of delay. The objective of this paper is to assess a model of care for patients with presbycusis that is both secure and effective in reducing waiting lists for patients with public health insurance. Hypothesis: more than 50% of the patients older than 65 years of age, with hearing loss, will have a symmetric high- frequency sensorineural hearing loss.

Material and methods:
Patients that attended the outpatient clinic of Otorhinolaryngology from Hospital Padre Hurtado complaining of hearing loss, between the months of June and November of 2022. All patients were subject to anamnesis, otomicroscopy, and tonal audiometry. Audiometric red flags: asymmetric hearing loss or the presence of an air-bone gap. Descriptive statistical analysis with SSPS. The protocol was approved by the local ethics committee.

Results:
We included 267 patients, 57.7% female, median age 77 years (range 65 to 100). Earwax prevalence 15.7% (IC 95% 11.6%, 20.6%), chronic otitis media prevalence 7.5% (IC 95% 4.5%, 10.9%). Presence of audiometric red flags: asymmetric hearing loss in 21.7% (IC 95% 17.2%-26.6%), air-bone gap in 12.4% (IC 95% 8.6%-16.5%). The prevalence of at least one red flag was 24.8% (IC 95% 19.5-30.1%).

Conclusion:
At least 69.9% of the patients had an audiometry with a typical pattern of presbycusis, and could safely dispense the evaluation by an otorhinolaryngologist specialist.

S20 L7 - Exploring Arctic Acoustics: Otology's Frontier in Greenland

Ramon Gordon Jensen
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Introduction:
The burden of hearing loss due to Chronic Suppurative Otitis Media (CSOM) is disproportionately high in developing regions and among First Nation populations. Despite this, basic understanding of the epidemiology, pathogenesis, and natural history remains scarce. Hearing loss (HL) resulting from CSOM can significantly impair communication abilities, hinder language development, and impede academic skills. This presentation aims to delineate advancements made in the last 15 years of research originating from one of the world's most remote regions—Greenland. From demonstrating and addressing the under-recognition of hearing loss through epidemiology to conducting implementation studies on transnational tele-audiology, the focus will encompass a comprehensive overview of these endeavors.

Methods:
Long-term follow-up of Greenlandic population-based children-cohorts was conducted, employing epidemiological, audiological, and qualitative research methods.

Results:
Among children with CSOM, 91% developed a permanent hearing loss of varying degrees. Over one-third of CSOM perforations healed spontaneously over time, highlighting the dynamic nature of the disease at both individual and community levels. The prevalence of hearing loss is underestimated among Inuit children, other First Nation populations, and in developing regions, attributed to older WHO definitions. Understanding the adaptation of families with multiple generations of untreated hearing loss necessitates collaboration and inclusion of native researchers in otology and audiology. The lack of access to specialists underscores the need for innovative solutions, pushing the boundaries of technological advancements.

Conclusion:
Advancing the public health agenda in resource-limited areas requires a multidisciplinary approach encompassing various fields of ontological research. Translational research aimed at shifting the public health focus to an otherwise silent and overlooked handicap is imperative.

Invited lecture – Prof. George Shambaugh
Promoting Innovation and Trust in Science without Borders

George Shambaugh
Georgetown University, Georgetown, USA

Thank you for the wonderful opportunity to share some thoughts about my grandfather, Dr. George E. Shambaugh, Jr.

One of my grandfather's most memorable characteristics was his ongoing interest in interacting, debating, and learning from others through the free, open, and inquisitive exchange of knowledge and research. He traveled extensively to observe techniques and interact with others. He was always asking questions and keen to learn about research in different fields. He continued to do research and publish papers long after all his other colleagues had retired. As reflected in his later exploration of the relationship between vitamin deficiencies and allergies on sensorineural hearing loss, tinnitus and other hearing issues, he never stopped exploring new ideas and was often ahead of his time. His curiosity and enthusiasm for a wide variety of areas inspired my academic career and interest in global affairs.

My grandfather used social interaction to inform his medical practice and research. This is reflected in his habit of devoting a half-hour or more to taking histories from patients before going to an exam room. A combination of careful listening, observation, and curiosity enabled him to connect dots between seemingly tangential behaviors and symptoms. It also inspired patients' confidence and trust, leading to relationships which sometimes lasted more than 60 years. These relationships were bolstered further by a monthly newsletter through which he shared information about new medical insights and ideas written in language layman could understand. The personal value he placed in relationships with patients and professional colleagues reflected his goal of always finding new ways to make people healthier. He died in his nineties as he was preparing to go to the office, having just renewed his medical license and the lease on his office.

I propose speaking about two themes built around his characteristics: medicine and science are most innovative when they have no borders, and are most effective when public confidence and trust in the science and the experts who apply it are high. These themes are particularly important today given the continued growth of extraordinary scientific and technological advancements and the countervailing rises of nationalism and public distrust of expertise in medicine. The latter is reflected most strikingly in the public backlash against vaccines during the COVID pandemic.

I am a political scientist and economist by training. One of my recent books, "Oracles, Heroes, or Villains: Economic Policymakers, National Politicians, and the Power to Shape Markets," models how the interactions between economic experts and national politicians affect market expectations and investor behavior before, during, and after economic crises. The ability to stabilize expectations about the efficacy and political viability of economic policy decisions is essential to restoring investor and consumer confidence. The challenge we face today regarding public distrust of experts, especially as revealed in anti-vaccination sentiments during the COVID pandemic, has some parallels to the distrust of economic experts during economic crises.

Lessons from those crises suggest ways that this confidence can be rebuilt. These include the promotion of cross-border collaborations to counter the growing tendency by national politicians to treat technological and scientific advances as proprietarycomponents of geo-economic competition among countries, and the rebuilding of public trust in science through the preservation of personal doctor-patient interactions and the explicit and public promotion of synergies between medical experts, national politicians, and other social cue givers designed to both validate and de-politicize science. I suggest the title: "Promoting Innovation and Trust in Science without Borders."

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FINAL PAGE – SPECIAL for CORLAS

De Auribus – 150 Years Vienna ENT University Department, 1873 – 2023

From Adam Politzer to HEARO Robot

A special exhibition created by Wolf-Dieter Baumgartner

Dear CORAS Members, dear guests and friends !

During our Annual Collegium meeting August 25-28, 2024 there is the chance to see the Vienna Medical History Museum in Währinger Strasse 25, 1190 Wien, for free. Just 18 minutes walk, 1200 meter away from our conference venue Palais Hansen.

With Your name bagde, no matter - if member, guest or accompanying person, You have free entrance to the Medical History Museum „Josephinum“ !

The Museum is open Wed 28th August to Sat 31st August, 10am to 6 pm. YOU CAN VISIT THE JOSEPHINUM on WEDNESDAY 28th August in between 10am and 6 pm for free. Please, do not forget Your name badge !

If You stay longer in Vienna, even after the Collegium Meeting, You have free entrance from Wednesday 28th to Saturday 31st August.

The „Josephinum“ itself is an outstanding landmark in medical history.
Once You are in Vienna it is actually a must see.

Prescribing Information

Fachkurzinformation zu Inserat GSK

Nucala 100 mg Injektionslösung im Fertigpen; Nucala 100 mg Injektionslösung in einer Fertigspritze; Nucala 40 mg Injektionslösung in einer Fertigspritze; Nucala 100 mg Pulver zur Herstellung einer Injektionslösung; Qualitative und Quantitative Zusammensetzung: Nucala 100 mg Injektionslösung im Fertigpen: Jeder 1-ml-Fertigpen enthält 100 mg Mepolizumab. Mepolizumab ist ein humanisierter monoklonaler Antikörper, der durch rekombinante DNA-Technologie in Ovarialzellen des chinesischen Hamsters hergestellt wird. Sonstige Bestandteile: Saccharose, Dinatriumhydrogenphosphat-Heptahydrat, Citronensäure-Monohydrat, Polysorbat 80, Natriumedetat (Ph.Eur.), Wasser für Injektionszwecke. Nucala 100 mg Injektionslösung in einer Fertigspritze: Jede 1-ml-Fertigspritze enthält 100 mg Mepolizumab. Mepolizumab ist ein humanisierter monoklonaler Antikörper, der durch rekombinante DNA-Technologie in Ovarialzellen des chinesischen Hamsters hergestellt wird. Sonstige Bestandteile: Saccharose, Dinatriumhydrogenphosphat-Heptahydrat, Citronensäure-Monohydrat, Polysorbat 80, Natriumedetat (Ph.Eur.), Wasser für Injektionszwecke. Nucala 40 mg Injektionslösung in einer Fertigspritze: Jede 0,4-ml-Fertigspritze enthält 40 mg Mepolizumab. Mepolizumab ist ein humanisierter monoklonaler Antikörper, der durch rekombinante DNA-Technologie in Ovarialzellen des chinesischen Hamsters hergestellt wird. Sonstige Bestandteile: Saccharose, Dinatriumhydrogenphosphat-Heptahydrat, Citronensäure-Monohydrat, Polysorbat 80, Natriumedetat (Ph.Eur.), Wasser für Injektionszwecke. Nucala 100 mg Pulver zur Herstellung einer Injektionslösung: Jede Durchstechflasche enthält 100 mg Mepolizumab. Nach der Rekonstitution enthält jeder ml Lösung 100 mg Mepolizumab. Mepolizumab ist ein humanisierter monoklonaler Antikörper, der durch rekombinante DNA-Technologie in Ovarialzellen des chinesischen Hamsters hergestellt wird. Sonstige Bestandteile: Saccharose, Dinatriumhydrogenphosphat-Heptahydrat, Polysorbat 80; **Pharmakotherapeutische Gruppe:** Mittel bei obstruktiven Atemwegserkrankungen, andere Mittel bei obstruktiven Atemwegserkrankungen zur systemischen Anwendung, ATC-Code: R03DX09. **Anwendungsgebiete:** Schweres eosinophiles Asthma: Nucala ist angezeigt als Zusatzbehandlung bei schwerem refraktärem eosinophilem Asthma bei Erwachsenen, Jugendlichen und Kindern ab 6 Jahren (siehe Fachinformation Abschnitt 5.1). Chronische Rhinosinusitis mit Nasenpolypen (*Chronic rhinosinusitis with nasal polyps*, CRSwNP): Nucala ist angezeigt als Zusatztherapie mit intranasalen Kortikosteroiden zur Behandlung von erwachsenen Patienten mit schwerer CRSwNP, die mit systemischen Kortikosteroiden und/oder chirurgischem Eingriff nicht ausreichend kontrolliert werden kann. Eosinophile Granulomatose mit Polyangiitis (EGPA): Nucala ist angezeigt als Zusatzbehandlung für Patienten ab 6 Jahren mit schubförmig remittierender oder refraktärer eosinophiler Granulomatose mit Polyangiitis (EGPA). Hypereosinophiles Syndrom (HES): Nucala ist angezeigt als Zusatzbehandlung bei erwachsenen Patienten mit unzureichend kontrolliertem hypereosinophilem Syndrom ohne eine erkennbare, nicht-hämatologische sekundäre Ursache (siehe Fachinformation Abschnitt 5.1). **Gegenanzeigen:** Überempfindlichkeit gegen den Wirkstoff oder einen der in der Fachinformation Abschnitt 6.1 genannten sonstigen Bestandteile. **Inhaber der Zulassung:** GlaxoSmithKline Trading Services Limited, 12 Riverwalk, Citywest Business Campus, Dublin 24, Irland. **Rezeptpflicht/Apothekenpflicht:** Rezept- und apothekenpflichtig, wiederholte Abgabe verboten. **Zulassungsnummer:** Nucala 100 mg Injektionslösung im Fertigpen: EU/1/15/1043/003 1 Fertigpen, EU/1/15/1043/004 3 (3 x 1) Fertigpens (Mehrfachpackung), EU/1/15/1043/007 9 (9 x 1) Fertigpens (Mehrfachpackung); Nucala 100 mg Injektionslösung in einer Fertigspritze EU/1/15/1043/005 1 Fertigspritze, EU/1/15/1043/006 3 (3 x 1) Fertigspritzen (Mehrfachpackung), EU/1/15/1043/008 9 (9 x 1) Fertigspritzen (Mehrfachpackung); Nucala 40 mg Injektionslösung in einer Fertigspritze: EU/1/15/1043/009 1 Fertigspritze, EU/1/15/1043/010 3 (3 x 1) Fertigspritzen (Mehrfachpackung); Nucala 100 mg Pulver zur Herstellung einer Injektionslösung: EU/1/15/1043/001, EU/1/15/1043/002. ***Weitere Angaben zu Warnhinweisen und Vorsichtsmaßnahmen für die Anwendung, Wechselwirkungen mit anderen Arzneimitteln und sonstigen Wechselwirkungen, Fertilität, Schwangerschaft und Stillzeit und Nebenwirkungen entnehmen Sie bitte der veröffentlichten Fachinformation.***

Ausführliche Informationen zu diesem Arzneimittel sind auf den Internetseiten der Europäischen Arzneimittel-Agentur https://www.ema.europa.eu verfügbar.

Stand der Fachkurzinformation: 06/2024

Die gültigen Fach- und Gebrauchsinformationen zu den GSK Produkten in Österreich finden Sie auf http://www.gsk-kompendium.at. Unerwünschte Nebenwirkungen melden Sie bitte an unsere Pharmakovigilanzabteilung; Tel.: +43 1 970 75 – 0; E-Mail: arzneimittelsicherheit@gsk.com

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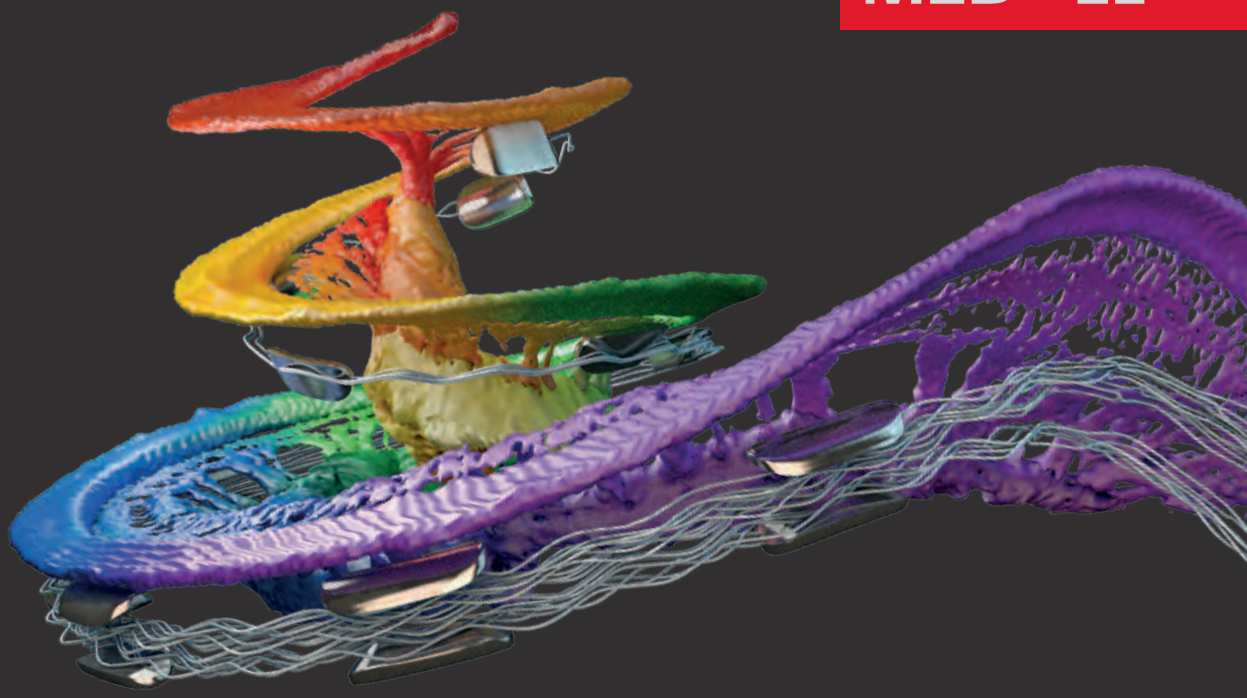

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