Organizers & supporters

Programme committee

- Anna Rossi, Communication Manager OIFE (Italy)
- Christer Zøylnner Swan, Associate professor, MD, PhD (Denmark)
- Dace Liepina, Vice President OIFE & Chair of LOIB (Latvia)
- Ingunn Westerheim, OIFE president (Norway)
- Jannie Hald, MD, PhD (Denmark)
- Kaija Kuurila-Svahn, MD, PhD (Finland)
- Lars Folkestad, MD, PhD (Denmark)
- Kristofer Andersson, DDS, PhD (Sweden)
- Taco van Welzenis, Honorary Member OIFE (The Netherlands)

The local organizing committee

- Dace Liepina, Chair of LOIB
- Kristiana Berzina, Member of LOIB
- Diana Ponaskova, Organizer

Meeting organization

- Osteogenesis Imperfecta Federation Europe (OIFE)
- Latvian Osteogenesis Imperfecta association (LOIB)

Sponsors & supporters

We are very grateful to the following organisations for their support. Without them the conference would not be possible.

Silver sponsor
Alexion

Exhibitors
Cast Print

Other supporters
Mereo Biopharma
Osteogenesis Imperfecta Foundation (OIF)
Ahuce
Association de l’Ostéogenèse Imparfaite (AOI)

Under the patronage of
EURORDIS
**Programme 2019**

**FRIDAY 14TH OF JUNE**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>09.00 - 10.30</td>
<td>Opening session</td>
<td>Moderators: Lars Folkestad &amp; Ingunn Westerheim</td>
</tr>
<tr>
<td>09.00 - 09.15</td>
<td>Welcome address</td>
<td>Kristofer Andersson, Dace Liepina, Ingunn Westerheim</td>
</tr>
<tr>
<td>09.15 - 10.00</td>
<td>Osteogenesis Imperfecta - an overview</td>
<td>Antonella Forlino</td>
</tr>
<tr>
<td>10.00 - 10.30</td>
<td>OI &amp; the teeth, eyes &amp; ears - a study of non skeletal phenotypes in adults</td>
<td>Bente Langdahl</td>
</tr>
<tr>
<td>10.30 - 10.50</td>
<td>Coffee break</td>
<td></td>
</tr>
<tr>
<td>10.50 - 12.50</td>
<td>Teeth, jaws &amp; OI</td>
<td>Moderators: Kristofer Andersson &amp; Ingunn Westerheim</td>
</tr>
<tr>
<td>10.50 - 11.00</td>
<td>Teeth &amp; OI - What are the challenges?</td>
<td>Anonymous patient testimonies</td>
</tr>
<tr>
<td>11.00 - 11.20</td>
<td>Oral &amp; craniofacial challenges in OI - a clinical overview</td>
<td>Kristofer Andersson</td>
</tr>
<tr>
<td>11.20 - 11.35</td>
<td>Prosthodontic treatment in OI</td>
<td>Ann Lindunger</td>
</tr>
<tr>
<td>11.35 - 11.50</td>
<td>Anti-resorptive therapy in OI vs. physiology and treatment of malocclusion</td>
<td>Manuel Joaquin de Nova García</td>
</tr>
<tr>
<td>11.50 - 12.05</td>
<td>Dental implants in individuals with OI: a 6-year follow-up study</td>
<td>Maung Maung Myint</td>
</tr>
<tr>
<td>12.05 - 12.20</td>
<td>The impact of OI on jaw function &amp; oral health-related quality of life</td>
<td>Hans Gjærup</td>
</tr>
<tr>
<td>12.20 - 12.35</td>
<td>Osteogenesis Imperfecta: a rare disease to consider in the differential diagnosis of hypophosphatasia</td>
<td>Agnès Bloch-Zupan</td>
</tr>
<tr>
<td>12.35 - 12.50</td>
<td>TAKO-centre - a multidisciplinary approach to oral health &amp; function in rare diseases</td>
<td>Stefan Axelsson</td>
</tr>
<tr>
<td>12.50 - 14.00</td>
<td>Networking lunch</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
<td>Speaker(s)</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>14.00</td>
<td><strong>Craniofacial issues &amp; OI</strong></td>
<td>Moderators: Antonella Forlino &amp; Dace Liepina</td>
</tr>
<tr>
<td>14.00-</td>
<td><em>Craniofacial issues &amp; OI - What are the challenges?</em></td>
<td>Anonymous patient testimonies (OIFE)</td>
</tr>
<tr>
<td>14.10</td>
<td><em>3D assessment of the craniofacial aspects of OI</em></td>
<td>Jean-Marc Retrouvey</td>
</tr>
<tr>
<td>14.50</td>
<td><em>Oral surgery and bisphosphonate treatment</em></td>
<td>Annika Rosén</td>
</tr>
<tr>
<td>15.10</td>
<td><em>Surgical correction of craniofacial anomalies in OI</em></td>
<td>Annika Rosén</td>
</tr>
<tr>
<td>15.30</td>
<td><em>Coffee break</em></td>
<td></td>
</tr>
<tr>
<td>15.50</td>
<td><em>Introduction to skull base abnormalities in OI</em></td>
<td>Janna Waltimo Siren</td>
</tr>
<tr>
<td>16.10</td>
<td><em>Symptoms &amp; management of basilar invagination in OI</em></td>
<td>Suken Shah (video lecture)</td>
</tr>
<tr>
<td>16.30</td>
<td><strong>Eyes &amp; OI</strong></td>
<td>Moderators: Antonella Forlino &amp; Ida Männistö</td>
</tr>
<tr>
<td>16.30-</td>
<td><em>Eyes &amp; OI - findings from a Danish study</em></td>
<td>Bente Langdahl</td>
</tr>
<tr>
<td>16.45</td>
<td><em>Eye diseases in patients with Osteogenesis Imperfecta, a register based nationwide cohort study</em></td>
<td>Lars Folkestad</td>
</tr>
<tr>
<td>17.00</td>
<td><em>Ocular changes in OI in a Portugese population</em></td>
<td>Rafael Barão</td>
</tr>
<tr>
<td>17.15</td>
<td><em>Break</em></td>
<td></td>
</tr>
<tr>
<td>17.35</td>
<td><strong>Poster pitching</strong></td>
<td>Moderators: Antonella Forlino &amp; Ida Männistö</td>
</tr>
<tr>
<td>17.35-</td>
<td><em>P1 - Dental satisfaction in children and young people with osteogenesis imperfecta</em></td>
<td>Jasmine May Cachia Mintoff</td>
</tr>
<tr>
<td>17.40</td>
<td><em>P2 - Study of the craniovertebral junction in the osteogenesis imperfecta patient</em></td>
<td>Nuria Gallardo-López</td>
</tr>
<tr>
<td>17.45</td>
<td><em>P3 - Morphological study of the dental structure with electronic scanning microscopy in a Spanish sample of patients with osteogenesis imperfecta</em></td>
<td>Andrea Martin-Vacas</td>
</tr>
<tr>
<td>Time</td>
<td>Event</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>17.50 - 18.00</td>
<td>Closure &amp; practical information</td>
<td></td>
</tr>
<tr>
<td>19.00 - 20.00</td>
<td>Welcome reception - See, Hear &amp; Smile to each other!</td>
<td></td>
</tr>
<tr>
<td>20.00 - 22.00</td>
<td>Networking dinner</td>
<td></td>
</tr>
</tbody>
</table>

**SATURDAY 15TH OF JUNE**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>09.00 - 10.20</td>
<td><strong>OI &amp; hearing loss - part 1</strong></td>
</tr>
<tr>
<td></td>
<td>Moderators: Christer Swan &amp; Anna Rossi</td>
</tr>
<tr>
<td>09.00 - 09.15</td>
<td>Welcome &amp; What are the challenges?</td>
</tr>
<tr>
<td></td>
<td>Anonymous patient testimonies (OIFE)</td>
</tr>
<tr>
<td>09.15 - 09.45</td>
<td>Hearing loss in OI - an overview</td>
</tr>
<tr>
<td></td>
<td>Freya Swinnen</td>
</tr>
<tr>
<td>09.45 - 10.00</td>
<td>Otological and audiological findings from the Danish study</td>
</tr>
<tr>
<td></td>
<td>Christer Swan</td>
</tr>
<tr>
<td>10.00 - 10.20</td>
<td>OI-related hearing loss in OI - follow up &amp; treatment</td>
</tr>
<tr>
<td></td>
<td>Freya Swinnen</td>
</tr>
<tr>
<td>10.20 - 10.40</td>
<td>Coffee break</td>
</tr>
<tr>
<td>10.40 - 12.40</td>
<td><strong>OI &amp; hearing loss - part 2</strong></td>
</tr>
<tr>
<td></td>
<td>Moderators: Lars Folkestad &amp; Taco van Welzenis</td>
</tr>
<tr>
<td>10.40 - 11.00</td>
<td>Surgical treatment options of hearing loss in OI</td>
</tr>
<tr>
<td></td>
<td>Ulrik Pedersen</td>
</tr>
<tr>
<td>11.00 - 11.15</td>
<td>Hearing aids improve hearing and a lot more - what users report</td>
</tr>
<tr>
<td></td>
<td>Max Niebling</td>
</tr>
<tr>
<td>11.15 - 11.30</td>
<td>Inner ear deafness &amp; OI - a solitary journey with a possible positive outcome</td>
</tr>
<tr>
<td></td>
<td>Diane Maroger</td>
</tr>
<tr>
<td>11.30 - 11.45</td>
<td>Cochlear implant surgery</td>
</tr>
<tr>
<td></td>
<td>Gunta Sumeraga</td>
</tr>
<tr>
<td>11.45 - 12.00</td>
<td>Break</td>
</tr>
<tr>
<td>12.00 - 12.15</td>
<td>OI &amp; hearing loss - how does it affect quality of life?</td>
</tr>
<tr>
<td></td>
<td>Tamara Fernandez</td>
</tr>
<tr>
<td>12.15 - 12.35</td>
<td>Hearing loss - psychological consequences &amp; coping techniques</td>
</tr>
<tr>
<td></td>
<td>Hege Saltnes</td>
</tr>
<tr>
<td>Time</td>
<td>Title</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>12.35 - 12.45</td>
<td><strong>O1</strong> - Study of the characteristics of dentinogenesis imperfecta in a sample of Spanish children with osteogenesis imperfecta</td>
</tr>
<tr>
<td>12.45 - 12.55</td>
<td><strong>O2</strong> Study of the dental development in Spanish children with osteogenesis imperfecta</td>
</tr>
<tr>
<td>12.55 - 13.05</td>
<td><strong>O3</strong> - Evaluation of the severity of malocclusion in Spanish children affected by osteogenesis imperfecta</td>
</tr>
<tr>
<td>13.05 - 13.15</td>
<td><strong>O4</strong> - Dental eruption chronology in Spanish children with osteogenesis imperfecta</td>
</tr>
<tr>
<td>13.15 - 13.25</td>
<td><strong>O5</strong> - An audit of the referral pathway for OI patients between Great Ormond Street Hospital and the Eastman Dental Hospital</td>
</tr>
<tr>
<td>13.25 - 13.30</td>
<td><strong>Closure &amp; goodbye</strong></td>
</tr>
<tr>
<td>13.30 - 14.30</td>
<td><strong>Grab &amp; go lunch</strong></td>
</tr>
<tr>
<td>14.30 - 18.00</td>
<td><strong>OIFE Annual General Meeting (for OIFE delegates &amp; invited guests)</strong></td>
</tr>
</tbody>
</table>
Antonella Forlino
Dr. Antonella Forlino is Associate Professor of Biochemistry at the Department of Molecular Medicine, Unit of Biochemistry, University of Pavia. She has a PhD in Biochemistry and the Speciality in Genetics. She spent 5 years of post-doc training in NIH, Bethesda, USA. Her research activity has been focused on the molecular, biochemical, and functional study of genetic diseases of the connective tissue in particular Osteogenesis Imperfecta (OI), using in vitro and in vivo models (mice and Zebrash). She is combining basic science with translational approaches. She is particularly interested on the intracellular effects of retained aberrant collagen type I in modulating the bone phenotype in both dominant and recessive OI.

Bente Langdahl
Bente Langdahl graduated in 1988 and did clinical training in internal medicine and endocrinology at Aarhus University Hospital. She received her PhD at Aarhus University in 1995: “Investigations on a possible pathogenic role of thyroid hormones in postmenopausal osteoporosis” and received a DMSc at the same university in 2004: ”The genetics of bone mass and risk of osteoporotic fractures”. In 2004 she was appointed consultant at the department of Endocrinology and Internal Medicine at Aarhus University Hospital and research lecturer at Aarhus University. She was appointed professor at Aarhus University in 2012. Her main research interests are identification and further investigation of genetic variants that imply increased risk of osteoporotic fractures, osteogenesis imperfecta in adult patients, interactions between fat and bone tissues, the impact of thyroid diseases and diabetes on bone health, the effects of vitamin D and K on bone metabolism, and the development of new treatments for osteoporosis.

Kristofer Andersson
Kristofer Andersson, DDS, PhD is currently in the final part of his postgraduate specialty training in pediatric dentistry at Karolinska Institutet, Huddinge. He has been a team member of the multidisciplinary national pediatric OI team at Astrid Lindgren Children’s hospital, Stockholm since 2013. In 2018 he defended his thesis Prevalence of dentinogenesis imperfecta and dental aberrations related to genetic findings in osteogenesis imperfecta.

Ann Lindunger
Ann Lindunger is a dental specialist in prosthodontics. She is working at the Eastman Institute in Stockholm, Sweden. She has been working with children and young patient who need prosthodontic treatment for 30 years and met several patients with dentinogenesis imperfecta and osteogenesis imperfecta during her time as a specialist. She also has lectures national and international about young patients and prosthodontic treatments.
Manuel Joaquin de Nova García

Dr. De Nova qualified as a doctor from the University Complutense of Madrid (UCM) (1990), and then became Specialist in Paediatric Dentistry. He has been a Professor in Paediatric Dentistry at the UCM in graduate and postgraduate activities. He is currently the Director for the MSc Paediatric Dentistry Program in the UCM. For the last two decades, he has participated in activities with related Associations (AHUCE and AMOI: Spanish associations of OI). As a result of the research interest in the OI, he has directed four PhD and seven final MSc projects. He is the academic and clinical lead for the Project “Contribution of oral and craniofacial repercussions to the current diagnosis of OI and its therapeutic modulation” jointly funded by the UCM and the AHUCE Foundation.

Maung Myint

Dr. Maung Myint is a special dentist at the National Resource Centre for Oral Health in Rare Diseases (TAKO-Centre), Lovisenberg Diaconal Hospital, Oslo, Norway. He earned his PhD in 1999 at the University of Oslo, Norway, for his work on immunological aspects of periodontal diseases in HIV-infected patients. Since 2002, he has been working in the field of Special Care Dentistry. He is the first author of the article “Dental implants in individuals with osteogenesis imperfecta: a 6-year follow-up study” that was accepted in March 2019 for publication in the journal Oral Surgery.

Hans Gjørup

Dr. Hans Gjørup is Head of Center for Oral Health in Rare Diseases, Dept. of Maxillofacial surgery, Aarhus University Hospital, Denmark. The formal education and academic training include DDS, Royal Dental College, University of Aarhus (1979), a specialist degree in Orthodontics from The School of Dentistry, Aarhus University (1990), and a Ph.D. from the Graduate School of Health, Aarhus University (2014). Previous employments and positions include private dental practice, private orthodontic practice, and head of orthodontic service in a public dental service. In addition, censor at pregraduate and at postgraduate training in orthodontics at universities in Denmark. The main focus in research has been orodental and craniofacial aspects of rare diseases of bone (hereditary rickets, osteogenesis imperfecta) in addition to oral health and oral health related quality of life in patients with dental anomalies.

Agnès Bloch-Zupan

Agnès Bloch-Zupan is a Professor in Oral Biology, Faculty of Dentistry, University of Strasbourg, France. She works in the Reference centre for rare oral and dental diseases and at the IGBMC research institute. Her activities are focused on orodental development and anomalies. She created original tools (patient database D4/phenodent, biological sample collection, NGS panel GenoDENT...). She is leading a European program Interreg V RARENET and is involved in the ERN CRANIO. She has more than 130 publications including 67 publications in peer reviewed journals; she gave 125 invited seminars and 160 presentations in congresses. She received in 2015 the prestigious Sciences Price of the Rhénane Académie and in 2016 the Micheline Blain Award, Canada. She is a Fellow of the Strasbourg Institute of Advanced Studies. She presides over the Scientific committee of Hypophosphatasia Europe.
Stefan Axelsson
Dr. Stefan Axelsson completed a specialist training in Orthodontics at the University of Oslo in 1991. He was then affiliated to the CLP-team at the National Hospital in Oslo and the Norwegian National Resource Centre for Special Education in Complex Speech, Language and Communication Disorders. Since 1993 he has been working at the National Resource Centre for Oral Health in Rare Medical Conditions (TAKO Centre) at Lovisenberg Diakonale Hospital, Oslo. His doctoral thesis “Variability of the Cranial and Dental Phenotype in Williams syndrome” was defended in 2005. He has written several scientific articles about oral health and craniofacial features in several rare syndromes. He has given many presentations, lectures and courses worldwide on subjects concerning craniofacial growth and development in rare syndromes as well as on orthodontic treatment for disabled children.

Jean-Marc Retrouvey
Jean-Marc Retrouvey, D.M.D, M.Sc. FRCD (C), is the director of the division of Orthodontics Canada and the new Director of the Graduate Orthodontic Program at McGill University in Montreal, as well as member of staff at the Montreal General Hospital and the Shriners Hospital while practicing orthodontics part time at the McGill Intra Mural Clinic. Dr. Retrouvey has been involved in the craniofacial research center at the Montreal Children Hospital, whose goal was to study the craniofacial characteristics of several syndromes, as well as being actively involved with the Montreal Shriners and McGill research group. He is the principal collaborator for the dental aspect of the Longitudinal Study of Osteogenesis Imperfecta and is the Principal Investigator for the “Dental Malocclusion and Craniofacial Development in OI” and has collaborated to a chapter on dental and craniofacial manifestations of OI in “Osteogenesis Imperfecta: A Translational Approach to Brittle Bone Disease,”

Annika Rosén
Annika Rosén has been since 2012 Professor at the Department of Clinical Dentistry at University of Bergen, Norway and Senior Consultant at the Department of Oral and Maxillofacial Surgery, the Head and Neck Unit at Haukeland University Hospital. She is especially experienced in orofacial pain, TMJ surgery and ortognathic surgery. She has built up a national unit/center for orofacial pain at the Haukeland University Hospital, and she is a leader of a research group, including several PhD students, Master students and research students. She was educated at the Karolinska Institutet, Huddinge, Sweden: DDS 1988, a doctoral degree in pharmacology, Dr Med Sci 1994, Specialist in Oral and Maxillofacial Surgery 2005, Associate Professor (Docent) 2007. She was the head of the Oral and Maxillofacial Surgery department at Karolinska Institutet from 2009-2012.
Janna Waltimo-Sirén
Janna Waltimo-Sirén (DDS, PhD) has a doctoral degree in dentistry from 1996 at University of Helsinki, Finland. Her doctoral thesis “Developmental defects of human dentin matrix. An ultrastructural study” covers several heritable diseases affecting dentin formation, OI included. She became a specialist in orthodontics in 1998 and a specialist in paediatric dentistry in 2017 at University of Helsinki. She has been nominated as Associate Professor (Docent) at two Finnish Universities, Turku and Helsinki. She holds a permanent position as university lecturer, teaching orthodontics at undergraduate and post-graduate levels, at the Department of Oral and Maxillofacial Diseases, University of Helsinki and Helsinki University Hospital. She also works part-time as private orthodontist. She has supervised four PhD theses, two of them being related to OI.

Suken A. Shah
Suken A. Shah, MD, Division Chief of the Spine and Scoliosis Center and Clinical Fellowship Director, is a pediatric orthopaedic surgeon at the Nemours/Alfred I. duPont Hospital for Children in Wilmington, Delaware and serves as Associate Professor of Orthopaedic Surgery and Pediatrics at Sidney Kimmel Medical College of Thomas Jefferson University. Dr. Shah is certified by the American Board of Orthopaedic Surgery. He is a researcher and key opinion leader in the field of spinal deformity surgery and performs advanced deformity correction techniques while also being a prolific writer (165 research publications, 22 book chapters) and serves as a reviewer for five medical journals. Dr. Shah is an active member of national specialty societies, serves on the Board of Directors of the Scoliosis Research Society as the Education Council Chair-elect and is a member of the Pediatric Orthopaedic Society of North America.

Lars Folkestad
Lars Folkestad is working as an associate professor and MD at the department of endocrinology at Odense University Hospital and Institute of Clinical Research at University of Southern Denmark. He has published several studies using the Danish Health Registries to evaluate the morbidity and mortality in patients with OI. He has been a part of the Bone and calcium metabolic diseases research unit at Odense University Hospital since 2005 and is part of both national and international research collaborations trying to better understand OI in the aging adult. He's a member of OIFE's Medical Advisory Board and a member of programme committee for See, Hear, Smile!

Rafael Correia Barão
Rafael Correia Barão, MD, MSc, received his medical degree from the University of Coimbra, with his masters' Thesis on the ophthalmologic phenotype in cobalamin errors. He is currently an Ophthalmology resident at Hospital de Santa Maria (Lisbon, Portugal), and an investigator with the Visual Sciences Study Center, Faculty of Medicine of the University of Lisbon.
Freya Swinnen
Freya Swinnen is audiologist at the Ghent University Hospital, Belgium. After obtaining her Master degree in Audiological Sciences at the Ghent University, she got involved in a research project on osteogenesis imperfecta, which was a collaboration between the Department of Otorhinolaryngology Nijmegen, The Netherlands, and the Department of Medical Genetics and Otorhinolaryngology of the Ghent University, Belgium. Based on OI family studies in Belgium and the Netherlands, in 2012, she presented her PhD thesis focusing on the audiological phenotype in OI patients and its correlation with the underlying genotype. At present, she’s responsible for audiological testing of cochlear implant candidates and their audiological rehabilitation. She gives lectures and practical sessions in the Master education of Audiological Sciences at the Ghent University. However, she’s still following the OI research from the sideline.

Christer Zøylner Swan
Christer Zøylner Swan is a consultant at the Department of Otorhinolaryngology and Head & Neck Surgery, Aarhus University Hospital, and also associate professor at the Department of Clinical Medicine, Aarhus University, both institutions located in Aarhus, Denmark. Professor Swan specializes in otology and otologic surgery, and contributed to the recent Danish study on non-skeletal phenotypes in osteogenesis imperfecta. He is also associated to the Center for Rare Diseases at Aarhus University Hospital, at which pediatric patients with OI are followed. With both a PhD and a clinical background from neurology, his areas of research are primarily related to diseases that affect the inner ear and central auditory pathways.

Ulrik Pedersen

Max Niebling
Dr. Max Niebling is a Policy Officer in the Secretariat of the European Hearing Instrument Manufacturers Association (EHIMA) and the German Federation of Hearing Instrument Manufacturers (BVHI). He is involved in awareness raising activities on occasion of World Hearing Day, the EuroTrak surveys on hearing loss and hearing aid usage and the networking with hearing-related interest groups all over Europe. He received his doctorate degree in political science from Technical University of Darmstadt. After working in Brussels, he entered the hearing instrument industry, in 2017.
Diane Maroger

Diane Maroger is a documentary film editor and director born with O.I type III in 1966 and graduated from the French national film school. Maternité interdite (Forbidden Motherhood), her first film co-produced by French national TV, was screened in festivals and broadcasted in various countries. She launched the first French Disability film festival, festival Retour d’image, which had four editions in major French cities. The project implied all films were audio-described and subtitled for blind and deaf audiences, and debates translated in sign language. In 2012 she produced a one shot national event on Disability and Film accessibility in collaboration with the Ministries of Culture and of Social and Health issues, and the French national Centre for film (CNC). Now an expert on film accessibility, she directed and produced a series of web-docs on the subject. She now works for a feature length production company called Decia Films.

Gunta Sumeraga

Dr. Gunta Sumeraga is the head of the Otorhinolaryngology department and assistant professor of Riga Stradiuns University. She is also the head and the leading surgeon of Otorhinolaryngology division of Pauls Stradins Clinical University Hospital. The main focus of her practical work is ear and skull base surgery, hearing restoration surgery, including cochlear implants.

Tamara Fernández

Tamara Fernández has been the psychologist of AHUCE (Spanish OI national organisation) since 2013. She offers psychological support, advice and counselling to OI patients and their families in order to improve their life quality. She also participates and organises meetings, workshops, talks and annual conferences about different OI topics. Since 2016 she has been part of the OI Multidisciplinary Unit from Sant Joan de Déu Hospital Barcelona.

Hege Saltnes

Hege Saltines is head of the Norwegian National Unit for Hearing Impairment and Mental Health. The unit has a nation-wide responsibility to diagnose and treat patients with a considerable hearing loss and mental illness. The National Unit consists of three units, one treating children and adolescents, one treating adults and one small unit for research and development. Hege Saltines is a senior psychiatrist who has been working in the field of mental health and hearing loss for many years. She has been specialized in cognitive behavioural therapy.
OI & the teeth, eyes & ears - a study of non-skeletal phenotypes in adults
Bente Langdahl

Bente Langdahl\textsuperscript{1}, Jannie Dahl Hald\textsuperscript{1}, Lars Folkestad\textsuperscript{2}, Christer Zøylner Swan\textsuperscript{4,5}, Jens Wanscher\textsuperscript{6}, Malene Schmidt\textsuperscript{7}, Hans Gjørum\textsuperscript{8}, Dorte Haubek\textsuperscript{7}, Christian-Heinrich Leonhard\textsuperscript{9}, Dorte Ancher Larsen\textsuperscript{9}, Jesper Østergaard Hjortdal\textsuperscript{9}, Torben Harsløf\textsuperscript{1}, Morten Duno\textsuperscript{9}, Allan M. Lund\textsuperscript{10}, Jens-Erik Beck Jensen\textsuperscript{11}, Kim Brixen\textsuperscript{2}

Affiliations
\textsuperscript{1}Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus
\textsuperscript{2}Department of Endocrinology, Odense University Hospital, Odense
\textsuperscript{4}Department of Otorhinolaryngology and Head & Neck Surgery, Aarhus University Hospital, Aarhus
\textsuperscript{5}Department of Clinical Medicine, Aarhus University, Aarhus
\textsuperscript{6}Department of ENT Head and Neck Surgery, Odense University Hospital, Odense
\textsuperscript{7}Section for Pediatric Dentistry, Department of Dentistry and Oral Health, Health, Aarhus University, Aarhus
\textsuperscript{8}Centre of Oral Health in Rare Diseases, Department of Maxillofacial Surgery, Aarhus University Hospital, Aarhus
\textsuperscript{9}Department of Ophthalmology, Aarhus University Hospital, Aarhus
\textsuperscript{10}Centre for Inherited Metabolic Diseases, Departments of Paediatrics and Clinical Genetics, Rigshospitalet, Copenhagen
\textsuperscript{11}Department of Endocrinology, Hvidovre Hospital, Hvidovre

Introduction
Osteogenesis imperfecta (OI) is a hereditary connective tissue disorder. The skeletal fragility is pronounced, however OI leads to a number of extra-skeletal symptoms related to the ubiquity of collagen type 1 throughout the human body. The vast majority of knowledge is derived from studies performed in the pediatric population. Thus, we aimed to investigate the nature and prevalence of ophthalmologic, odontologic and otologic phenotypes in an adult population with OI.

Methods
The study population comprises 85 Danish OI patients (age: 44.9±15.9 years). Fifty-eight patients had OI type I, 12 OI type III, and 15 OI type IV according to the classification by Sillence. Audiometric evaluations and dental examinations were performed in 62 and 73 patients, respectively. Ophthalmologic investigations were performed in 64 patients, including measurements of the central corneal thickness.

Results
All patients, except two, had corneal thickness below the normal reference value. Patients with OI type I and patients with a quantitative collagen defect had thinner corneas compared to patients with OI type III and other patients with a qualitative collagen defect. Three patients in this cohort were diagnosed with glaucoma. Dentinogenesis imperfecta was diagnosed in one fourth of the patients, based on clinical and radiographic findings. This condition was predominately seen in patients with moderate to severe OI.

Hearing loss requiring treatment was found in 15 of 62 patients, of whom three were untreated. The most prevalent type of hearing loss (HL) was sensineural HL, whereas conductive HL was solely seen in patients with OI type III. The patients with the most severe degrees of HL were patients with mild forms of OI. Age was associated with increased HL.

Conclusion
Although significant health problems outside the skeleton are frequent in adult patients with OI, the patients are not consistently monitored and treated for their symptoms. The reason for this is unknown. However, differences in the general approach to management of OI in pediatric and adult patients may play a role.
Clinicians treating adult patients with OI should be aware of non-skeletal health issues, and consider including regular interdisciplinary check-ups in the management plan for adult OI patients.

**Oral and craniofacial challenges in osteogenesis imperfecta – a clinical overview**

**Kristofer Andersson**

Osteogenesis imperfecta (OI) is a heterogeneous connective tissue disorder, mainly characterized by growth retardation and an increased tendency to fractures. In more than 80% percent of cases, the disorder is caused by mutations in the collagen type I genes, *COL1A1* and *COL1A2*. Collagen type I is the main organic component of skeletal bones, but also of several oral tissues. The dentin (the tissue located under the enamel) has many similarities with bone tissue. More than 90% of the organic component in dentin is collagen type I. Using a metaphor, collagen type I acts like the reinforcing bars in concrete. The mineralization of the teeth relies on the presence of this meshwork. Consequently, it is not surprising that individuals with OI, also often present with specific challenges related to tooth and craniofacial development.

For many years it has been known that the dental aberration dentinogenesis imperfecta (DI or DGI) is a common manifestation in OI. DGI is characterized by a varying degree of discoloration. Due to the soft, dysplastic dentin, the enamel chips off, thus exposing the dentin. These teeth are prone to attrition and fractures, resulting in an increased risk for occlusion disturbances. The presence of discoloration may also be an esthetic problem. These features give rise to several indications for restorative and prosthodontic treatment.

Later studies have also concluded that other dental aberrations are common in OI. Congenital missing teeth (tooth agenesis), tooth eruption problems (retention/impaction), and taurodontism are some of these that have to be diagnosed at an appropriate age and treated. The aberrant collagen type I also manifests in the craniofacial bones, causing specific growth patterns. Orthodontics alone or combined with orthognatic surgery may be necessary in order to achieve a functional occlusion. The knowledge of the specific tooth and craniofacial development in OI is crucial in optimal treatment planning and treatment. This presentation will give an introduction to the oral and craniofacial challenges encountered in OI.

**Prosthodontic treatment in OI**

**Ann Lindunger**

Dentinogenesis imperfecta is a common manifestation in osteogenesis imperfecta. The teeth exhibit a varying degree of discoloration and tendency to fractures. There is an extensive individual variation. The root canal (pulp) is often wide initially, but gradually becomes more narrow, a process called obliteration. If a tooth with dentinogenesis imperfecta is infected, the obliteration makes root canal treatment more complicated. When teeth with dentinogenesis imperfecta exhibit smaller fractures, conventional restorations can be done, but in cases with more extensive fractures or bite forces, ceramic crowns can be necessary. In cases with esthetic concerns, ceramic veneers may be the best treatment option. In sporadic cases we have replaced missing teeth with dental implants and implant bridges. In those cases we have used longer periods for bone healing before permanent treatment.
**Anti-resorptive therapy in osteogenesis imperfecta vs physiology and treatment of malocclusion**

Manuel Joaquin de Nova Garcia

The antiresorptive treatment (bisphosphonates) which has changed the natural history of osteogenesis imperfecta (OI) can be considered in the orofacial field as a potential risk for associated physiological processes, such as dental development and eruption, and even as a potential enemy of our therapies. The bisphosphonate therapy has shown to be beneficial for the skeletal system and spinal column, (Cochrane Database Syst Rev 2009, 2014). Contrary to this, the dental specialties watch with concern the most recent advances (incorporation of more potent bisphosphonates (zoledronic acid)), for its greater potential interference in both events, dental development and eruption.

Several studies with animal experimentation have already confirmed how the administration of some bisphosphonates delays the dental eruption of rodents. This is due to its action, related to the interference in the osteoclasts activation. Together with the eruptive delay, some researches have also revealed some defects of dental development. Precisely, most recent studies, with more potent bisphosphonates (zoledronic acid) emphasize even more in these dental development abnormalities (Hiraga et al 2010). On this basis, there are some on-going studies on the interaction between the cells involved in both processes; bone resorption and dental and periodontal development (Gama A et al, 2015).

The clinical implication of aforementioned findings extrapolated to children with OI has been poorly documented, and existing ones are related to teeth eruption and the administration of less potent bisphosphonates. However, there is a clear message for the dentist who treats children with OI, this is; they must individualise the treatment effects on the physiology of the oral cavity. Moreover, their observations, shared with clinicians (pediatricians, endocrinologists), can contribute to the therapeutic modulation of the protocol with bisphosphonates.

The experience shows there is a need to carry out an exhaustive control of the dental development and eruption since the dentist often needs to intervene by extracting retained primary teeth. On top of this, it has been observed in some cases, serious deviations from normality, which are difficult to explain, and could possibly have a treatment implication.

Bisphosphonates have also been shown to interfere with dental treatments and in particular with those in which dental movement is involved, as dental treatment to correct malocclusions.

In OI patients, the class III malocclusion (dental and skeletal) is prevalent (above 60%). This is secondary to an alteration of the craniofacial development (Waltimo J et al, 2005) (hypoplastic maxilla, prognathic mandible in anterior rotation and poorly developed alveolar bones). This disruption would explain why the Class III malocclusion prevalence increases in the most severe types of the disease (OI type III), and why they also require surgical treatment (orthognathic surgery) for the correction of the underlying skeletal disorder.

The use of specific assessment indexes objectifies a greater severity of malocclusion (Rizkallah J et al, 2013), which could already be clinically identified in patients with OI. In our experience and with control subjects also class III, we have obtained much higher scores of discrepancy index (DI) in subjects with OI. The variable of the DI that affect the most the severity of a malocclusion are lateral open bites and "others" which includes agenesis, ectopic eruption and deviation of the middle line.

Although an increase in malocclusion has been reported as children with OI, there is little known about its characteristics in primary dentition. We are not aware of any related studies.

In addition, the knowledge of its treatment comes from a scarce and anecdotal caseload, which has prioritised the effect of dentinogenesis imperfecta and the treatment of the more complex cases with orthognathic surgery (Harstfield JK et al 2006). Recently there have been reports of other treatment experiences such as
orthopedic therapy with rapid maxillary expansion (RME) in patients with osteogenesis imperfecta and treated with bisphosphonates (Ierardo G et al, 2015).

The greater severity of malocclusion in the OI patients, the effect of bisphosphonates on dental movement is added, this increases the complexity of orthodontic treatment in these patients.

Again, animal experimentation has confirmed the effect of bisphosphonates on dental movement (Iglesias A et al, 2010). Initially these effects were considered beneficial, considering it a favourable anchorage, and as a control of unwanted dental movements. However, its extrapolation to orthodontic treatment in humans has shown problems. Since the initial concerns were raised (Schwartz JE, 2005), new cases have been reported where difficulties associated with dental movement have occurred in adults treated with bisphosphonates (Arbelaez ML et al, 2018). It is striking that until today the majority of the caseload is from older patients.

Although in 2009 Ramalingam L and Zacharin M raised through an abstract of the unusually prolonged orthodontic treatment in children who have received bisphosphonates, a more recent and specific publication on therapeutic approaches on oral manifestations of OI (Rousseau et al, 2018), does not even mention such this possibility in the treatment of malocclusion. This study gives greater relevance to osteonecrosis of the jaws as a possible complication of the use of bisphosphonates in these patients. In this publication they confirm, "Not enough clinical data is available about outcomes of orthodontic treatments in moderate to severe OI subjects to issue clear treatment guidelines on intervention at an early age may be best."

Our experience with children in orthodontic treatment who are receiving treatment with bisphosphonates (pamidronate and zoledronic acid) shows that in addition to a prolonged treatment time, what could be considered as an ankylosing dental response has been observed. This not only makes the closure of open lateral bites impossible, but it helps to accentuate them in some patients. Taking into consideration these difficulties and on the basis that malocclusion in children with OI worsens over time, we develop the philosophy that an early intervention can be effective in achieving some objectives and / or facilitating a subsequent correction of the malocclusion. Based on the principles of neuro occlusal rehabilitation (RNO) we have initiated an early treatment in children aged 4-5 years (temporary dentition). We incorporated traction with facial mask in older children (mixed dentition) and we reflected on the progress and difficulties associated with a more traditional orthodontic treatment approach.

In order to anticipate the clinical difficulties, it would be interesting to see new contributions to the study of Jabbour et al (2018), genotype-phenotype correlation, in which they conclude that the Type of disease-causing mutation affects the severity of malocclusion in individuals with OI

Based on the increasing amount of information available (clinical, genetic, biochemical, pharmacological) it is necessary to create research and researchers networks in order to establish protocols that facilitate the clinical care of professionals with less experience, and contribute to improve the dental care to this group.

Dental implants in individuals with osteogenesis imperfecta: a 6-year follow-up study
Maung Maung Myint

Background
Except from a few case reports, no long-term study on the success rate of dental implants in a group of individuals with osteogenesis imperfecta (OI) had been reported.

Objective
To perform a long-term follow-up of a previous prospective study in a group of individuals with OI after a mean observation time of 1.5 years.
**Methods**

The previous study included seven participants (20 implants), of whom four participants (11 implants) agreed to take part in the present study. Three former participants had died. The participants were followed-up for average of 93 months subsequent to prosthetic loading. The implants were clinically and radiographically examined. Subjective and objective evaluations were recorded using an analogue scale ranging from 0 as the worst to 10 as the best score. A mean of these evaluations is presented as an indicator of subjective and objective overall satisfaction.

**Results**

At the previous study, no implants were lost and 1 mm bone loss was recorded around two implants. One implant was removed after 76 months due to an implant-neck fracture. At the present study, two implants showed 4 mm peri-implant bone loss and four other implants showed 1 mm peri-implant bone loss. No bone loss was observed around the remaining four implants. Subjective and objective evaluations of implant treatment showed an overall high satisfaction of 9.9 and 9.1, respectively.

**Conclusion**

The findings showed an implant survival rate of 91% (100 %, excluding the implant-neck fracture) and high recipient satisfaction towards implant treatment in these individuals with OI.

---

**The impact of OI on jaw function and oral health-related quality of life**

**Hans Gjørup**

**Introduction**

Osteogenesis imperfecta (OI) is a rare inherited disease characterized by brittle bones. Both mild and severe forms exist. The individuals with OI often experience pain and broken bones, and the patients with the severe OI-types develop short stature and severe skeletal malformation. OI occurs due to a defect in the formation of collagen, which is the dominant protein of bone and a significant part of the dentine of teeth. Thus, OI may also impact on both teeth, in terms of dentinogenesis imperfect (DI), and jaws, in terms of malocclusion or fracture of jaws. Teeth with DI are fragile and extensive dental treatment might be a necessity. In addition, a malocclusion, if present, may initiate impaired jaw function. In total, it might be expected that OI influences the oral health related physical, psychological and social well-being of the affected individuals.

**Aim**

The aims of the lecture are to present results from 1) studies on the occurrence of temporomandibular disorders (TMD) in adults with OI and 2) studies on oral health related quality of life in patients with OI in comparison with another rare skeletal disorder. In addition, it is the aim to demonstrate the benefits of a close collaboration between dental and medical professionals in research on rare diseases.

**Study population and methods**

Part 1. The participants in the study on jaw function were 75 adults with OI, which all had mutation in COL1A, and they were classified with mild OI (n=56) or moderate-severe OI (n=19). Dental occlusion was assessed on clinical photos and 3D models. The participants were examined according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD). In the analyses, the group of mildly affected individuals were compared with the moderately-severely affected individuals.

Part 2. The oral health-related quality of life was assessed in the same OI group (n=75) by the participants’ answering of a standardized questionnaire, Oral Health Impact Profile (OHIP49). The questions and results of OHIP are grouped into 7 domaines (functional limitation, pain, psychological discomfort, physical, psychological, and social disability, and handicap). The results in the OI group was compared with a group of adults (n=36) with X-linked Hypophosphatemia (XLH). XLH is a rare hereditary disease characterized by insufficient bone mineralization because of renal phosphate depletion. Reference values were mean OHIP values in a previous study, which included 30 Swedish adults without chronic disease.
Results
Part 1. Mandibular overjet and posterior cross-bite were more prevalent in moderate-severe than in mild OI group (P < 0.050). Temporomandibular disorders and functional limitations in the orofacial region were rare and did not differ between patients with mild and moderate-severe OI (P > 0.050). Myofascial pain was rare in both groups. Disc displacement and other joint diagnosis were rare, and the difference in the occurrence between groups was minimal. Reduced jaw opening was more prevalent in moderate-severe than in mild OI (P = 0.037). No significant differences between Graded Chronic Pain Scale grades 0, 1, and 2 were found in mild OI vs. moderate-severe OI (P > 0.160). Few patients (16%) had signs of depression, but close to half (48%) had signs of somatization.

Part 2. In the comparison of OHIP between OI and XLH groups, the mean (sd) OHIP score was in OI: 21.2 (19.7) and in XLH: 36.3 (26.3). Reference OHIP value = 9.3 (6.3). Medians of domain scores in OI respective XLH were: Functional limitation (OI=3; XLH=6.5), pain (OI=5; XLH=9.5), psychological discomfort (OI=2; XLH=5.5), physical disability (OI=1; XLH=4), psychological disability (OI=0; XLH=2), social disability (OI=0; XLH=0), handicap (OI=0; XLH=2). The relative domain score is greater for functional limitation, pain, and psychological discomfort than for domains on disability and handicap, which is in accordance with the relative distribution of domain scores in the reference group.

Conclusion
Mandibular overjet and posterior cross-bite were more prevalent in adults with moderate-severe OI than in adults with mild OI. The psychosocial status in the OI group was remarkably healthy considering the severity of the disabling systemic disorder in the group. The bodily pain complaints frequently reported in OI patients were not reflected in the orofacial area.

Both adults with OI and adults with XLH experience impact on oral health-related quality of life. Oral health-related quality of life in individuals with XLH is more severely affected than in patients with OI.

Osteogenesis imperfecta: a rare disease to consider in the differential diagnosis of hypophosphatasia
Agnès Bloch-Zupan

Background
Hypophosphatasia (HPP, [OMIM] #146300, 241500, 241510, ORPHA:436) is a rare inherited progressive metabolic disease in which mutations in the ALPL gene (encoding tissue-nonspecific alkaline phosphatase TNSALP) result in varying degrees of enzyme deficiency and mineralisation deficit affecting the bones and teeth. HPP manifests in a spectrum of skeletal (rickets, skeletal deformity, poor healing or recurrent fractures, fractures/pseudofractures, osteomalacia...) and non-skeletal symptoms, including early primary tooth loss (before 3 years of age with a root intact) and alveolar bone mineralization defects. Its differential diagnosis includes osteogenesis imperfecta.

Objectives
The aim of this presentation is to provide an overview of HPP to raise disease awareness and aid its recognition. A special focus will be made on orodental anomalies encountered in HPP comparatively to dental defects associated to osteogenesis imperfecta.

Methods
Patients were examined at the Centre de Référence des Maladies Rares Orales et Dentaires (CRMR O-Rares), Strasbourg, France or within the O-Rares network. The oral phenotype was documented using the D[4]phenodent registry protocol, a Diagnosing Dental Defects Database [see www.phenodent.org, for assessment form], which is approved by CNIL (French National commission for informatics and liberty, number 908416). This clinical study is registered at https://clinicaltrials.gov: NCT01746121 and NCT02397824, and with the MESR (French Ministry of Higher Education and Research) Bioethics
Commission as a biological collection "Orodental Manifestations of Rare Diseases" DC-2012-1677 within DC-2012-1002 and was acknowledged by the CPP (person protection committee) Est IV December 11th 2012. Patients and non-affected family members gave written informed consents in accordance with the Declaration of Helsinki, both for the D[4]/phenodent registry and for genetic analyses (GenoDENT) performed on the salivary samples included in the biological collection.

Results
Orodental repercussions of HPP are reported in all forms of the disease, and concern every mineralized tissue from cement and alveolar bone to dentin and enamel leading to early loss of primary/permanent teeth but also to dentin and enamel defects. The comparison of dental hallmark between HPP and osteogenesis imperfecta could help differential diagnosis.

Conclusion
A better knowledge of the oral manifestations associated to different skeletal dysplasias can therefore contribute to improve early diagnosis and management of those conditions.

This work was financed by and contributed to the actions of the project No. 1.7 “RARENET: a trinational network for education, research and management of complex and rare disorders in the Upper Rhine” co-financed by the European Regional Development Fund (ERDF) of the European Union in the framework of the INTERREG V Upper Rhine program as well as to the ERN (European reference network) CRANIO initiative. Agnès Bloch-Zupan received support from Alexion.

TAKO-centre – a multidisciplinary approach to oral health og function in rare diseases
Stefan Axelsson

The term oral health comprise more than having healthy teeth and gums. It also includes oral and facial functions necessary for breathing, eating, speaking, and communication. Clinical experience and research reveal that challenges with oral health and orofacial functions are frequent among individuals with rare diagnoses. Continuity in the oral health care and oral motor training and stimulation are necessary for many patients in order to maintain good oral health and adequate functions throughout life. Further, there is a reciprocal effect between oral conditions and general health. Interdisciplinary collaboration over organizational boundaries within community and specialized healthcare systems is therefore very important for individuals with rare diagnoses.

The TAKO-centre was established more than 25 years ago as the first resource centre for oral health in rare diagnoses in the Nordic countries. The TAKO-centre was soon followed by similar resource centers in both Sweden and Denmark, six centres altogether. The multidisciplinary approach to oral health has been central in both clinical work and research projects. Different dental specialists are collaborating together with speech and language therapists and physiotherapist internally at the TAKO-centre as well as together with medical units at the hospital and the Dental Faculty, University of Oslo, located nearby. Close collaboration with the other eight resource centres within in the Norwegian Advisory Unit on Rare Disorders (NKSD) has also been essential.

Teaching is, besides clinical work and research, the third leg of the major tasks for the TAKO-centre. The staff at the TAKO-centre uses considerable time in teaching and disseminate knowledge about oral health and orofacial function to students in the dental and dental hygienist programmes at undergraduate level as well as dentists within the specialist programmes. Knowledge about dental health and orofacial function is continuously presented to groups of individuals and their caregivers at courses and gatherings within the NKSD organization and at separate meetings for the different diagnosis/syndrome associations. Several times yearly, the TAKO-centre is inviting to continuing education courses and gatherings for dental and medical personnel. The research activities at the TAKO-centre has been considerable during the years with three doctorate theses on oral health in various rare syndromes produced with in the centre and in collaboration with the Dental
Faculty, and continuous ongoing multidisciplinary research collaboration within the hospital, with other resource centres and with the Dental Faculty. From the very beginning the TAKO-centre have had a clinical and research focus on oral health in Osteogenesis Imperfecta with research projects on e.g. the morphology on dental enamel and the dentine-enamel junction (Lindau et al., 1999), later on the oral health in adults (Sæves et al., 2009), and recently on dental implants (Myint et al., 2011 and 2019).

3D assessment of the craniofacial aspects of OI

Jean-Marc Retrouvey

Osteogenesis Imperfecta subjects present significant craniofacial, occlusal and dental implications. As OI affects all hard tissues, cranial bones and the dentition are frequently affected to various degrees.

The whole craniofacial complex is affected, and frequently function and esthetic are compromised.

Patients may present with triangular faces, low ears, significant malocclusion with a severe decrease in maxillary development and rotation of the mandible resulting in a prognathic profile.

The dental occlusion of OI patients presents very specific traits that are seldom found in unaffected patients. Lateral open bite, a condition where the posterior teeth fail to meet at the occlusal plane, reduces the masticatory capabilities and anterior and posterior crossbite further complicate the masticatory function.

There is a significant lack of understanding of the craniofacial and dental growth patterns and development of OI patients. Combined with the reluctance of dental providers to get involved in patients taking IV bisphosphonates, many OI patients do not receive orthodontic treatment that could potentially reduce their masticatory impairment as well as improve their facial esthetics. On the other hand, some orthodontists disregard the special needs of OI patients and treat them as unaffected patients. This situation often results in poor outcomes which may compromise the future quality of life of OI patients.

This presentation will focus on exploring the craniofacial aspect of OI patients and will present potential therapeutic approaches that could be developed to improve QOL in OI patients.

Oral surgery and bisphosphonate treatment

Annika Rosén

Osteonecrosis of the jaws (ONJ) after antiresorptive therapies is a serious complication in patients with osteoporosis, certain types of cancer (breast-, prostate and myeloma cancer) or autoimmune diseases. The medications are bisphosphonates, denosumab (monoclonal antibodies) or certain chemotherapeutic drugs. Bisphosphonates inhibit the digestion of bone by encouraging osteoclasts to undergo apoptosis, or cell death, thereby slowing the bone loss. Denosumab binds directly to the RANKL receptor and inhibit osteoclasts activity.

The condition was discovered 2003 and the incidence is increasing worldwide. The prevalence of ONJ in patients medicated with bisphosphonates is more common among patients with cancer, up to 27.5%, with osteoporosis up to 4.3%. Women are more exposed, 2/3, mean age 65-68 years (range 35-95).

ONJ can lead to loss of teeth and/or bone in the jaw and decrease the function and quality of life. The mandible is more exposed, twice as frequently affected than the maxilla. About 60% of cases are preceeded by a dental surgical procedure. Exposed bone or a fistula recognizes ONJ in the jaws, but a number of patients have
unexposed bones making it more difficult to diagnose. The clinical examination together with imaging, such as CT, CBCT, Scintigraphy, will give the diagnosis.

Tooth extraction in patients with low doses of antiresorptive therapy may be performed in general dental care, but patients should be monitored until healing occurs. Tooth extraction on patients with high doses of antiresorptive therapy should be referred to an Oral and Maxillofacial Surgery clinic. ONJ in the jaws can be in 50% of the cases treated successfully with surgery.

The lecture will present guidelines from the network of the Scandinavian ONJ Cohort for how to take care of patients before and during antiresorptive therapy to prevent ONJ, and present guidelines for treatment of patients with established ONJ.

References:

Surgical correction of craniofacial anomalies in osteogenesis imperfecta
Annika Rosén

Osteogenesis imperfecta (OI) is an inherited genetic disorder, and known as ‘brittle bone disease. The incidence is 6–20 per 100,000 newborns. Medical treatment for OI includes calcitonin, sodium fluoride, growth hormone, cortisone, anabolic steroids, vitamins C and D, minerals and bisphosphonates. The most effective treatment is bisphosphonates, which minimize osteoclast activity. The side effects are unknown in patients with OI. In the light of the increasing development of bisphosphonate-associated osteonecrosis, the dental status of OI patients should be monitored and appropriate precautions should be planned for.

A Class III malocclusion is seen in 75% of adults with OI. The malformation of the face, with subsequent malocclusion and wrong jaw positioning, such as a retrognathic maxilla and a prognathic mandible, can be corrected by orthodontic and maxillofacial surgical interventions. Orthognathic surgery in OI patients is rare but most cases result in a successful outcome with stable and good occlusion.

Prior to orthognathic surgery, it is important to consider several surgical and anaesthetic issues. Bone and teeth fractures easily, so precautions have to be taken during anaesthetic procedures. Small fractures in the bone have been reported during a Le Fort I osteotomy. Vascular disorders or impaired platelet aggregation are common and can lead to bleeding peri- or postoperatively. In some cases, excessive perioperative or postoperative bleeding, due to the collagen deficiency in the vessels, has been reported. There are also risks of metabolic defects perioperative, for example, OI patients experience a greater incidence of hyperthermia with general anaesthesia, which can develop into malignant hyperthermia. There may also be intubation difficulties due to the patient’s short neck, large tongue and thoracic deformity, which may result in respiratory dysfunction. Cardiac abnormalities may also be present such as valvular incompetence or septal defects.

Two male patients, 22 and 26 years old, with severe types III and IV of OI, and malocclusion class III with retrognathic maxilla and prognathic mandible, were treated with orthodontic treatment and bimaxillary surgical correction.
In conclusion, it is possible to perform combined orthodontic and orthognathic surgery in patients with OI despite the greater risk of complications than in patients without. The treatments were successful with follow up times of 5–6 years.

Reference

Introduction to skull base abnormalities in OI
Janna Waltimo-Sirén

The skull base and craniovertebral junction area between the base of the skull and superior part of the spine may display morphological deviations from normal as an inborn malformation or related to diseases. Various types of skull base abnormalities are not infrequent in patients with OI, particularly with severe OI types. The most common abnormality is called platybasia, which means a flat skull base. It is diagnosed from a conventional lateral skull radiograph, or from MRI or CT midsaggital plane section, as an abnormal obtuse angulation, larger 146 degrees, between the two planes drawn from 1) center of the pituitary fossa to the fronto-nasial suture and 2) from pituitary fossa to the anterior edge of foramen magnum. Platybasia appears to develop early, possibly prenatally, and as such has not been associated with symptoms. It is, however, most prevalent in severe OI types and often co-insides with clinically more important types of craniovertebral pathology, namely basilar impression and basilar invagination.

Basilar impression refers to relative lowering of the head in relation to the spine. It is diagnosed when vertebral structures protrude abnormally high above the borders of the skull. In practice, the distance of the odontoid process tip is measured to reference planes drawn from the distal palate to the lowest cranial point behind foramen magnum (=McGregor’s line) or to the posterior lip of the foramen magnum (=Chamberlain’s line). Other measurements have been developed more recently. The normal reference values are age-dependent. Basilar impression is often associated with shortening or bending of the clivus and increased curvature of the brainstem. Whereas basilar impression can cause impingement on the brainstem and spinal cord and affect cerebrospinal fluid flow, these problems and consequent neurologic problems are more probable in basilar invagination. This refers to a status where the foramen magnum becomes partially obstructed by intruding uppermost vertebral structures.

Basilar impression and basilar invagination have been observed in some patients with OI from the age of 2 years onwards. There is some scientific evidence to suggest that early-onset bisphosphonate treatment delays development of craniovertebral junction pathology, but it may appear despite the treatment. OI patients with scoliosis and short stature are prone to display some form of skull base abnormality, whereas hearing loss or the common joint hypermobility do not implicate an increased risk.

Symptoms & management of basilar invagination in OI
Suken A. Shah (video lecture)

Osteogenesis imperfecta (OI) is a genetic disorder of type I collagen. Type I collagen is located mainly in bone, ligaments, dentin and sclerae. There are multiple genotypes and phenotypes associated with OI; about 90% of the mutations are in the COL1A1 and COL1A2 genes. OI is characterized by bone fragility and patients typically present with multiple fractures or limb deformity; however, the spine of patients with OI can also be affected. Spine manifestations of OI include scoliosis, kyphosis, craniovertebral junction problems and spondylolisthesis in the lumbosacral spine. The early use of bisphosphonate treatment has been shown to be beneficial for the extremities and the spine by decreasing progression of scoliosis and improving bone quality. Patients should be screened with a clinical exam, including neurologic exam and a lateral cervical spine x-ray by school age to
identify silent craniocervical junction abnormalities such as basilar impression. The incidence of lumbosacral spondylolysis and spondylolisthesis is higher in OI than the general population. Contemporary operative techniques such as traction, pedicle screw instrumentation, cement augmentation and use of antibibrinolytics to decrease blood loss have advanced the treatment of these children with severe spinal deformity. The importance of early identification of scoliosis, kyphosis and craniocervical junction problems cannot be over emphasized.

**Eyes & OI - findings from a Danish study**

_Bente Langdahl_

_Bente Langdahl², Jannie Dahl Hald¹, Lars Folkestad³, Christian-Heinrich Leonhard⁴, Dorte Ancher Larsen⁹, Jesper Østergaard Hjortdal⁹, Torben Harsløf³_

**Affiliations**

¹Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus
²Department of Endocrinology, Odense University Hospital, Odense
³Department of Ophthalmology, Aarhus University Hospital, Aarhus

**Introduction**

Osteogenesis imperfecta (OI) is a hereditary connective tissue disorder. The skeletal fragility I pronounced, however OI leads to a number of extra-skeletal symptoms related to the ubiquity of collagen type 1 throughout the human body. The vast majority of knowledge is derived from studies performed in the pediatric population. Thus, we aimed to investigate the nature and prevalence of ophthalmologic, odontologic and otologic phenotypes in an adult population with OI.

**Methods**

The study population comprises 85 Danish OI patients (age: 44.9±15.9 years). Fifty-eight patients had OI type I, 12 OI type III, and 15 OI type IV according to the classification by Sillence. Ophthalmologic investigations were performed in 64 patients, including measurements of the central corneal thickness.

**Results**

The prevalence of bluish coloured sclerae was 90%. The mean CCT±SD was 473±38µm. With the exception of two patients (both OI type IV), CCT was below the normal reference value, (550±30.1µm, mean±SD) (p<0.001). Patients with OI type I had a mean CCT of 461±32µm. In patients with OI type III and OI type IV, CCT was 510±29µm and 500±40µm, respectively (p<0.001). Because of the marked difference in CCT between patients with OI type I and healthy controls, we investigated the ability of CCT to discriminate these two populations. Based on sensitivity and specificity we constructed a receiver operating characteristics (ROC) curve and the area under the curve was 0.98 suggesting that CCT is a very strong diagnostic test. By inspecting the coordinates we found that the optimal threshold was a CCT of 505µm giving a sensitivity for diagnosing OI type I of 97.6% with a specificity of 94.3%. Mean anterior chamber depth was 2.73±0.36mm in the cohort, without significant differences between the three groups, or between patients with quantitative and qualitative collagen defects. Three patients (OI type I) were diagnosed with glaucoma, two with primary glaucoma and one with acute glaucoma.

**Conclusion**

Diagnostic challenges may occur in mild OI. Based on the results obtained in the present study, we suggest using an ophthalmologic examination with CCT measurement in the case of an uncertain diagnosis of OI type I. Thus, a very low CCT may turn out to be an important sign of OI. With a confirmed diagnosis of OI, ophthalmologic investigations may be needed to out rule glaucoma. These findings, however, needs to be replicated in another and preferably larger population.
Eye diseases in patients with Osteogenesis Imperfecta, a register based nationwide cohort study.

Lars Folkestad

Lars Folkestad1,2, MD, Phd, Malin Lundberg Rasmussen1, MD, Phd and Jannie Dahl Hald4, MD, Phd
1) Department of Endocrinology, Odense University Hospital 2) Institute of Clinical Research, University of Southern Denmark 3) Department of Ophthalmology, Odense University Hospital 4) Department of Endocrinology, Aarhus University Hospital

Introduction:
In the eye, collagen type 1 is an important component of the scleral stroma, the layers of the cornea, and the uveal tissues. In OI, conditions like myopia and astigmatism are commonly reported. Even though, previous studies have shown that OI patients in general have thinner corneas than healthy controls and case reports have described traumatic scleral rupture, retinal detachment, and hemorrhages in patients with OI, the risk of eye diseases in OI is unknown. The Danish health registers include information about discharge diagnosis, drug use and operation types on an individual level. The Danish National Patient Register (NPR) coverage (covers or has a coverage) above 99% of all hospital contacts, and the overall positive predictive value of a diagnosis in the register is above 95%. The Danish healthcare system is uniform, tax-financed, and covers all residents. Together, these conditions allow near complete ascertainment and long-term follow-up of clinical conditions even with low base-rates. We hypothesize that patients with OI will have increased risk of glaucoma, refraction abnormalities, cataract and retinal detachment compared to the general population.

Methods:
We included all registered patients with OI from 1977 to the end of 2012 and a matched reference population of otherwise healthy individuals. The reference population was matched 5:1 to each OI patient on birth year, birth month and sex. We used relevant ICD-8, ICD-10, procedural codes and ATC codes to identify relevant eye diseases from the health registers. Accepting that a patient was diagnosed with a given disease the day they were entered into the NPR or picked up a prescription for a relevant drug. We used Fine and Gray competing risk regression to calculate the sub-hazard ratio between the patient cohort and the reference population. Accepting a SHR to be significant if the 95% CI did not include 1.00. All analysis were done via a remote desktop at Statistics Denmark’s Division of Research computers. All statistical analysis were done using Stata version 14.2.

Results:
We identified 687 patients with OI and 3435 individuals comprise the reference population. There were an increased incidence of glaucoma (2.9% vs 1.3%, SHR 2.12 [95% CI 1.25-3.59]), refraction abnormalities (2.3% vs 0.5%, SHR 4.15 [95% CI 2.11 – 8.19]), retinal detachment (1.2%. vs 0.1%, SHR 12.2 [95% CI 3.22 – 46.25]) and cataract (5.7% vs 2.4%, SHR 2.23 [95% CI 1.50-3.32]). Patients with OI were registered with a given diagnosis for glaucoma, refraction abnormalities and cataract at a much younger age than the reference population.

Conclusion:
Even though the absolute risk of eye diseases was low, there seems to be an increased risk of glaucoma, refraction abnormalities, retinal detachment and cataract in patients with OI.
Ocular Changes In Osteogenesis Imperfecta in a Portuguese Population

Rafael Barão

Background
Osteogenesis imperfecta (OI) is a connective tissue disorder that mainly affects the musculoskeletal system but can present with manifestations in other organs and tissues. The most commonly reported ocular findings are the presence of blue sclerae, corneal thinning, high refractive errors, an increased risk for glaucoma and other anterior segment abnormalities such as keratoconus. Other less frequently reported manifestations include an increased risk for scleral rupture, posterior staphylomas, choroidal neovascularization, retinal haemorrhaging and detachment. These descriptions have often been based on isolated case reports and small series, and the prevalence and severity of these ophthalmologic manifestations has not been systematically studied.

Objectives
To assess the visual function and identify ocular changes in a Portuguese population of adult OI patients. Additional objectives include exploring relationships between clinical OI types and ocular phenotypes and other subanalysis of the results that may be relevant.

Methods
Ongoing cross-sectional observational study. So far, twenty-seven adult patients (22 female) diagnosed with OI, with an average age of 44 ± 16 years, have voluntarily enrolled. Study visit included complete ophthalmological evaluation, including undergoing best corrected visual acuity (BCVA) testing, automated refractometry, intraocular pressure (IOP) measurement, corneal tomography, biomicroscopy and fundus retinography. Additional clinical data, such as phenotyping and genetic classification was retrieved from patient files.

Results
All twenty-seven patients have been clinically diagnosed with OI. Of these, 25 have had a definitive phenotyping classification and only 20 have been genetically characterized. Out of those patients who were clinically classified, 16 were OI type I (64%), 4 OI type IV (16%), 3 OI type III (12%), 1 OI type VI and 1 OI type VII (4%). COL1A1 gene mutations were found in 17 patients (85%), and mutations in the COL1A2, SERPINF1 and CRTAP genes were found in one patient each. Most patients (21/27) were found to have lower than normal central corneal thickness (CCT) and two patients (one OI type IV and one unclassified) had thick corneas. Overall mean CCT for both eyes was 481 ± 57 µm, which was significantly lower than a reference range of 550 ± 30 µm (p < 0.001), and an association between thinner corneas and the presence of blue sclerae was found (p=0.001). Mean BCVA was 0.1 ± 0.2 logMAR for both eyes. Mean refractive errors for both eyes was -1.0 ± 5 diopters (D) of sphere and -1.2 ± 0.9D cylinder, and six patients had high-grade refractive errors. IOP measurements for both eyes did not differ significantly, on average being 13 ± 4 mmHg, and were positively correlated with central corneal thickness (r=0.7, p < 0.0001). Blue sclerae was present in 19 patients (70% of total), and both OI type VI and VII patients did not present with blue sclerae. Five patients had bilateral keratoconus (two of them previously diagnosed) and fourteen patients were found to have tomographically-suspect corneas. We found no other relevant anterior or posterior segment findings with could be directly attributed to OI. No patient in this cohort has been diagnosed with glaucoma. However, standard automated perimetry and OCT imaging was not undertaken.

Conclusions
OI has a definite and clinically significant impact on ocular structure and visual function. We found a high prevalence of clinically significant refractive errors in this sample, with an overall myopic shift, as well as a high prevalence of keratoconus and suspicious corneas, with the overwhelming majority of patients displaying thinned corneas. Due to sample size and to the preponderance of OI type I individuals and COL1A1 mutations in this population, thus far we were unable to draw significant associations between clinical OI types and ocular
Hearing loss in osteogenesis imperfecta: an overview
Freya Swinnen

Hearing loss has been mentioned as one of the triad of symptoms of osteogenesis imperfecta (OI), together with blue sclerae and bone brittleness. Based on large population studies in different countries, it appears that hearing loss affects about half of the OI population. Different types of hearing loss with different pathophysiology and different site-of-lesion characteristics have been diagnosed in OI. It manifests often bilaterally and affects male and female patients to the same proportion. OI-related hearing loss commonly arises as a conductive hearing loss in the second to fourth decade of life and evolves to a mixed hearing loss thereafter. The underlying pathology is a bone remodeling process affecting the oval window region in the temporal bone. This aberrant process initially causes stapes footplate fixation corresponding with a pure conductive hearing loss, but proceeds to involve pericochlear temporal bone areas, which results in concomitant inner ear deterioration and, hence, a mixed hearing loss.

Besides conductive and mixed hearing loss, a pure sensorineural hearing loss of, yet unknown, underlying pathogenesis is observed in a minority of OI patients. It may arise at any age and is usually less progressive than the conductive/mixed type of hearing loss in OI.

Based on family studies including 184 OI patients, originating form 89 independent families, with genetically confirmed autosomal dominant OI between 2008 and 2011 in The Netherlands, Italy and Belgium, we concluded that the development of OI hearing loss is not associated with the overall disease severity as it affected patients with a mild phenotype as well as physically severely disabled patients. In addition, the OI-related hearing loss develops independently of the underlying OI genotype, as no correlation was observed between the occurrence or type of the hearing loss and the mutated gene, the nature of the type I collagen defect or the location of the mutation in the gene. Relatives harboring an identical mutation causing OI demonstrate variability with regard to the occurrence and type of hearing loss. Consequently, besides the mutation in \textit{COL1A1} or \textit{COL1A2}, an additional genetic trigger is assumed to be responsible for the manifestation of hearing loss in OI.

Otological and audiological findings from the Danish study
Christer Zøylner Swan

Osteogenesis imperfect (OI) is known to cause hearing loss (HL). 62 (73%) of the 85 patients included in the Danish study on non-skeletal phenotypes in OI, underwent evaluation of hearing function, including otologic evaluation and audiometry.

The results of the study, including the distribution of types and severity of HL will be presented, along with their relationship to both OI type and collagen type 1 defect sub-group, will be presented.

Further, patient files were scrutinized to determine type of surgery performed previously, and results on hearing post-surgery will also be provided and discussed.
**OI-related hearing loss: follow-up and treatment**

**Freya Swinnen**

The progression of OI-related hearing loss over time has been investigated by a cross-sectional study with 182 OI patients resulting in age-related threshold audiograms (ARTAs) for patients with hearing loss of the conductive/mixed type and for patients with the pure sensorineural hearing loss type separately. In the patients with a conductive/mixed hearing loss type, average threshold deteriorations for air conduction of 0.6 dB/year at mid-frequencies and 0.8 dB/year at higher frequencies, together with an 0.4 dB/year for bone conduction were reported. Therefore, the progression is mainly dominated by sensorineural deterioration due to the involvement of inner ear structures and pericochlear bone in the pathological bone remodeling process, whereas it initially only affects the stapes footplate. In the patients with pure sensorineural hearing loss, the average threshold deterioration was 0.2 dB/year for the mid-frequencies and mounted up to 1.2 dB/year at 8 kHz. Comparison of the ARTAs for conductive/mixed hearing loss with those for pure sensorineural hearing losses from 40 years yield differences in progression, severity, and audiometric configuration between both hearing loss types. The age-related bone conduction thresholds of the mixed hearing loss type exceed the thresholds of the pure sensorineural losses from the age of 40 years onwards, implying a more destructive inner ear pathology in the OI patients with mixed hearing loss compared to those with pure sensorineural hearing loss.

On the basis of a longitudinal study in which OI patients were audiologically evaluated at two time points with an average test time interval of 4 years, audiometric evaluation in the OI population is recommended every 3-4 years and should include oto-acoustic emissions in addition to pure-tone audiometry, in order to detect early conductive hearing loss. Tympanometry and acoustic stapedius reflexes are less informative since the results are difficult to interpret due to the often thin, hypermobile eardrums related to the type I collagen defect.

In the more frequently occurring conductive or mixed type of hearing loss, stapes surgery may be considered for reducing or eliminating the conductive hearing loss component. Even though, in the past, stapes surgery has been considered to be risky in OI patients because of the fragile or atrophic middle ear ossicles, a thickened, brittle stapes footplate and hypervascularized mucosae, today it may be appreciated as a valuable technique improving hearing in a considerable part of hearing-disabled OI patients, especially when being performed by an experienced otologic surgeon. The presence of a sensorineural hearing loss component may not be a contraindication to stapes surgery, since the benefits of stapes surgery are in most cases persisting for several years.

Other treatment option for OI-related hearing loss are hearing aids, bone-anchored hearing aids. In rare cases of complete deafness, cochlear implantation may be considered.

**Surgical treatment options of hearing loss in OI**

**Ulrik Pedersen**

Operative findings and results of stapedectomy in 32 patients (43 ears) with OI is presented. It is a historic material from the nineteen eighties from all over Denmark. It is still one of the biggest materials internationally published about surgery of the hearing loss in OI.

The stapes footplates were in may ears thick and of a very soft consistency. In all operated ears we found the stapes footplates fixated in the oval window. Brittle and atrophic stapes crurae were a common finding, but in only 5 ears fractures of the crura was observed.

A thick and vascular middle ear mucosa was seen in several ears. Although the middle ear proved quite different from that of otosclerosis, no major difficulties and no serious complications occurred during stapedectomy. Histopathological examination revealed an otospongiosis-like lesion in most of the footplates.
The bony structure was usually immature in varying degrees, and the bony tissue was reminiscent of the osteogenic structure found in the peripheral bones of OI patients. The histologic appearance was not like that in otosclerosis.

Both the immediate postoperative hearing gain and the long-term hearing results were, in general, satisfactory. Our study supports both the statement of previous publications and of recent publications, that stapedectomy and stapedotomy in Osteogenesis Imperfecta is a safe and reasonable alternative to hearing aids.

---

**Hearing aids improve hearing and a lot more – What users report**

**Max Niebling**  
*European Hearing Instrument Manufacturers Association (EHIMA)*

EuroTrak is the largest comparative multi-country study on hearing loss and hearing aid usage. Initiated by the European Hearing Instrument Manufacturers Association (EHIMA) in 2009, EuroTrak was designed as a means for raising public awareness on key issues of hearing loss and hearing care. It sheds light on hearing loss prevalence as well as on the use of hearing aids and the experience of hard of hearing people with their hearing instruments.

EuroTrak is an online panel study. Initially conducted in Germany, France and United Kingdom, EuroTrak today covers 14 European and non-European countries. Repeating a national survey every three years allows to identify trends across time and borders.

One in ten of the total EU population states a hearing loss. Only one in three of the hard of hearing people use hearing instruments. Hearing loss prevalence among people with Osteogenesis Imperfecta is even higher. Treating hearing loss is vital. Hearing instruments do not only improve hearing – but a lot more. Based on users’ experiences, the presentation highlights the impact of hearing instruments on peoples’ life. Hearing aid users report a better health, a better performance at work and an overall better quality of life compared to hard of hearing people with an untreated hearing loss.

---

**Inner Ear deafness and OI — a solitary journey with a possible positive outcome**

**Diane Maroger**

In this five parts presentation I will begin by explaining (1) how sounds and a talent for communicating with words were two key elements in my early life and career. I will then proceed to explain (2) how I found out about my own deafness — at age 30, just as I was ending film school —, how doctors and other professionals presented the situation, how I adapted to external hearing aids and how I reacted psychologically. I will evoke (3) what I learnt about deafness and how I met the Deaf signing community first, before I met the “becoming deaf” community and its very specific problems. I will speak about how different it is to have inner ear degeneration or middle ear hearing defect, how little patients with O.I in France really know about this and the possible causes. I will talk of what gradual hearing loss implies in addition to a physical disability — the degradation of work and social relations —, and how important it was, at age 51, to be able to connect with OIFE to get some encouragement and face the possibility of having a cochlear implant. In part 4, I will focus on my preparation for implantation, evaluating the risks, and on how patient feedback and surgeon testimonies helped me, and on how time with the medical team in charge evolved until I actually felt ready to undergo of surgery. Finally, the joys of partial “hearing recovery” will not be overlooked (5), knowing however that they were prepared and nourished also, by twenty years of actively reminding myself of the beauty of sounds, by four years of lip reading training and by working closely on accessibility with other technical aids,
Cochlea implants & OI
Gunta Sumeraga

Cochlear implant surgery
There could be many types and variation in the severity of the hearing loss in patients with Osteogenesis imperfecta (Pillion et al., 2008). In the case of severe sensorineural hearing loss, the cochlear implantation could be the solution.

First, the cochlear implantation was invented in 1957 by André Djourno and Charles Eyriès as single electrode device, then by William House in 1961 and by Blair Simmons and Robert J. White 1964 (Swirsky et al., 2017). Later in the late seventies, the new multichannel cochlear implant was introduced to the market with great success. Nowadays, approximately 324,200 registered cochlear implant has been implanted worldwide (US. Department of Health & Human Services, 2017).

Device: Cochlear implant has two parts - the inner part and the outer part (speech processor). The inner part consists of the electrode and the corpus. The inner part of the cochlear implant is inserted via surgery in the temporal bone of the patient - the electrode goes inside the cochlea to provide electrical impulses directly to the nerve fibres of the cochlear nerve, the corpus part is embedded and fixed in the mastoidal part of the temporal bone. The surgery is done under general anaesthesia.

The outer part of the cochlear implant or so-called speech processor looks similar to the hearing aid. However, there are now also different types on the market (Rondo by MedEl and Kanso by Cochlear) and consists of the microphone, a receiver/stimulator, which receives signals from the speech processor and converts them into electric impulses, battery pack, magnet coil. Both parts are connected via magnet through the skin of the patient providing electrical impulses directly to the cochlear nerve fibres.

The indications for the cochlear implantation is severe sensorineural hearing loss. The implantation could be done unilateral or bilateral.

The challenging situations regarding patients with Osteogenesis imperfecta during cochlear implantations would be related to the structural changes of the bone resulting in difficulties to drill bone bed for the corpus of the cochlear implant and to fix it properly. Also, the surgeon must carefully study the images of the cochlea and choose the right length and type of the electrode, expecting the possible narrowing or ossification of the cochlear channels.

Despite the small numbers of publications related the cochlear implantation in the case of osteogenesis imperfecta, the cochlear implantation would be a method of choice to restore hearing in the case of severe sensorineural hearing loss (Makizumi et al., 2013; Rotteveel et al., 2008; Streubel and Lustig, 2005; Migirov et al, 2003; Szilvássy et al., 1998; Huang et al., 1998).

OI & hearing loss - how does it affect quality of life?
Tamara Fernandez

Osteogenesis imperfecta (OI) is the most common heritable disorder of connective tissue. It is associated with fractures following relatively minor injury, blue sclerae, dentinogenesis imperfecta, increased joint mobility, short stature, and hearing loss.
Progressive hearing loss is one of the principal symptoms of OI, affecting about 50% of adult patients. It may also occur in childhood and results in additional disability in education and psychosocial adaptation and aggravates the physical handicap.

Hearing loss is often described as an invisible disability. It can lower a person’s quality of life, and can have far-reaching psychological, physical and social consequences, especially if it is left untreated for any length of time.

The effect of hearing loss on day-to-day functioning is seen in activities of daily living at home, at work, and in social or business situations. The potential consequences of hearing impairment may include:

- Experience a range of emotions: shame, guilt, denial, anger, embarrassment, worry, and frustration.
- Communication problems: in general, hearing loss makes communication with the outside world difficult. People often need to learn new ways to interact in the world to increase their involvement. They also have difficulty participating fully in conversations at work, home and in social situations.
- Introversion and social withdrawal: hearing loss progresses slowly and, over time, people who have it tend to begin withdrawing from social situations that prove too challenging. As the ability to hear deteriorates, many people find themselves withdrawing from social interactions, avoiding groups and strangers.
- Sadness or depression.
- Anxiety: for the hearing impaired, trying to keep up in conversations and overcoming the anxiety of being in social settings is very stressful.
- Low self-confidence and self-esteem.
- Fatigue: normal interactions require tremendous attention, listening becomes a multi-sensory task, involving a much greater level of visual and general attention than it does for those with normal hearing.
- Problems with concentrating.
- Employment: hearing impairment may have an impact on choice of vocation, or result in discrimination or negative attitudes towards a hearing impaired person. A person may find it difficult to obtain and retain employment because of hearing impairment or deafness is seen as a disability requiring special concessions.
- Recreational: hearing loss may mean that the person cannot participate in activities in which hearing plays a critical part, for example some sports, music, choir, drama. The presence of related conditions, for example tinnitus and balance problems, can limit the ability to participate in sport.

The experience of hearing loss is different for everyone, that why it is essential to attend every person individually and explore their particulars. The first step should be the test of these mentioned potential consequences in order to personalize the psychological intervention.

**Hearing loss - psychological consequences & coping strategies**

**Hege Saltines**

Hearing loss is common in individuals with osteogenesis imperfecta (OI). Studies report prevalence of HL ranging from 46 to 95%. Some reports that it is infrequent among children, other studies report that hearing loss is found also in young age.

Hearing loss can be conductive (involving the ossicles, ear drum, and middle ear) or sensorineural (involving cochlea, auditory nerve and brain), or a combination of both.

The etiology of hearing loss is unclear, but is assumed to be a consequence of the combination of atrophy of hair cells and abnormal bone formation in the cochlea and anatomical surroundings. Conductive hearing loss can be due to footplate fixation. The treatments most often referred to are surgical procedures and cochlear implantation.
This presentation focuses on the communicative challenges of hearing loss, the potential psycho-social consequences of hearing loss, and strategies of coping.

Hearing enables us to communicate and to become aware of potentially dangerous situations. *Communication* is demanding for individuals with hearing loss. It takes additional effort and extra concentration is needed. This can be explained by how the working memory operates. With hearing loss more of a persons’ working memory is occupied with perceiving what is said, and the person needs extended time to understand the content of a message. Always being a little delayed in listening is exhausting over a longer period of time. The brain is always working at a higher speed.

With hearing loss it will take more mental capacity to distinguish the sounds from each other, and to interpret them as meaningful. With normal hearing this usually takes no effort.

When the hearing is reduced, maybe only fragments of what is said is perceived, and to understand it is necessary to actively fill in the meaning-gaps, this requires an additional mental effort as well.

You can compare a person with hearing loss with a smart phone that has a lot of apps open. It needs frequent recharging because it uses a lot of energy. This may be an illustration of how it is to have a hearing loss. Accordingly, you have to find your appropriate “charging method”.

In addition it is demanding to *constantly be monitoring danger*. With normal hearing one can trust the senses and relax. If something unusual is heard, smelled, seen, felt or tasted, the sympathetic nervous system prepares for fighting or fleeing. When one or more of the senses are not fully working, one have to be more alert all the time. This is energy consuming and for some individuals, stressful.

Why talk about an extra amount of energy use in the context of hearing loss and mental health? We think it is uttermost important to understand the implications for well-being to grasp the consequences of the hearing loss on expenditure of daily energy. When having OI it can seem irrelevant to deal with a small hearing loss, but it is not!

If the person with a hearing loss do not understand the extra effort it takes how the world around can be expected to understand?

If a person is not recharging adequately he or she can be exhausted, and this again can lead into a situation more prone to develop anxiety and depression and other mental health issues.

Having a hearing loss or being deaf is not giving the origin of a certain mental health status. Being hard of hearing does not give a certain diagnosis. People with hearing loss are having the same mental illnesses as others, but as a consequence of the difficulties with communication we see increased vulnerability to develop mental illness.

Researchers are pointing out that degree of perceived communication difficulties is more likely to predict mental health problems than degree of hearing loss.

**Coping strategies:**
- Be aware of the consequences of the hearing loss
- Find a charging station (or two or three)
- Be a teacher (learn the surroundings how to facilitate)
Abstracts

ORAL COMMUNICATIONS

O1
Study of the characteristics of dentinogenesis imperfecta in a sample of Spanish children with osteogenesis imperfecta
Andrea Martín Vacas
Paediatric Dentistry, Universidad Complutense de Madrid (UCM), Madrid, Spain
Co-authors: Joaquín de Nova-García, Alejandra Hernández-Guevara, Andrea Castellanos-Guerrero, Pilar Gutiérrez-Diez

Background
Dentinogenesis Imperfecta (DGI) type I is the hereditary defect of dentine that is associated with Osteogenesis Imperfecta (OI), constituting a frequent finding in patients with OI. Traditionally, great heterogeneity has been described both in the manifestations of DGI-I and in its severity, but there is no established consensus about whether the severity of dental involvement is associated with the severity of systemic involvement.

Objectives
The main objective is to study the clinical and radiographic characteristics of dental anomalies present in the deciduous and permanent dentition in a sample of children with OI. The specific objectives are: 1. To examine the clinical and radiographic anomalies of the deciduous and permanent dentition in a sample of children with OI with photographic and radiographic records. 2. To relate clinical and radiographic characteristics. 3. To study the relationship between the involvement of the deciduous and permanent dentition. 4. To establish the possible differences in dental anomalies according to the type of OI.

Methods
This is a retrospective analytical observational study based on intraoral photographic images and radiographic records (orthopantomographies) of 31 subjects under 18 ages diagnosed with OI, classified according to Silince classification. We collected the characteristics of the DGI at the clinical-radiographic level that had been previously described by other authors, and analysed the relationship with the type of OI through statistical tests (Chi square test and Fisher's exact test) with a confidence level of 95% (p <0.05). This work has been carried out with the support and financing of the collaboration agreement Fundación AHUCE-UCM.

Results
The clinical manifestations of DGI-I are more frequent in the primary dentition (92%) while the radiographic ones are more usual in the permanent dentition (93.5%). The most frequent clinical findings are the discoloration and the appearance of bulbous crowns; and the radiographic findings pulpal obliteration and accentuated cervical constriction. Clinical and radiographic signs of DGI-I were not related in the deciduous dentition, but they were in the permanent one (p 0.049), finding that all the patients with clinical signs are affected at the radiographic level. We studied the relationship between the signs of DGI-I in the deciduous and the permanent dentition, finding that while in the clinical signs they were not related (p 0.099), the 95.5% of children with radiographic alterations in the permanent dentition had been affected at this point in the deciduous dentition (p 0.005). Regarding the relationship with the type of OI, in the case of deciduous dentition it could be established that the severity of attrition (p = 0.035) and pulp obliteration (p = 0.011) was related to the severity of the systemic affection, being more frequent in subjects with a more severe OI phenotype; that relationship can’t be established in the rest of the variables studied, neither in the permanent dentition.

Conclusions
DGI-I has a very heterogeneous manifestation, being a great variability both intra and intersubject. Clinical signs of DGI-I are more frequent in the deciduous dentition than the permanent one, but the permanent dentition is more affected at the radiographic level. There is evidence that the radiographic signs are maintained with the eruption of the permanent teeth, although the relationship can’t be established with the clinical signs. There is not relationship between the clinical and radiographic signs of OI and the systemic phenotype, although dental attrition was more frequent in the OI type III and IV in the deciduous dentition, and the pulp obliteration were
presented more often in OI type III in the permanent dentition.

O2 Study of the dental development in Spanish children with osteogenesis imperfecta
Andrea Castellanos-Guerrero
Postgrad In Pediatric Dentistry / Universidad Complutense De Madrid, Madrid, Spain
Co-authors: Helen Pamela Pasapera-Santos, Gonzalo Feijóo-García, Andrea Martín-Vacas, Joaquín de Nova-García

Background
Osteogenesis Imperfecta (OI) is a heterogeneous hereditary disorder of the connective tissue characterized, clinically, by the fragility and the increase of the susceptibility to the fractures, being its origin genetic mutations in one of the two genes (COL1A1, COL1A2) that codify the type I collagen. The prevalence of OI is approximately 1/15,000 to 1/20,000 newborns, affecting equally both sexes, races and ethnic groups. The clinical severity varies widely from almost asymptomatic with a slight predisposition to fractures, to profoundly disabling and even lethal. The most common skeletal manifestations are fractures of long bones, fractures of vertebrae are also observed. The deformities in the extremities are characteristic, as well as the short stature and the presence of severe scoliosis. Regarding dental structures, various alterations have been described, such as dentinogenesis imperfecta, alterations in dental development, hypodontia, taurodontism, dental retentions and malocclusions of various types. Bisphosphonates (Bs) are the treatment of choice in patients with OI because they improve bone mineral density and reduce the number of fractures. It is not a curative treatment, Bs are part of a coordinated multidisciplinary treatment, however, adverse effects have been reported such as alterations in dental development, tooth eruption and mineralization of dental tissues.

Objectives
The objective was to estimate the dental age of a sample of children with different types of OI, to relate it to their chronological age and to compare the results with two control samples (Canadian from Demirjian et al. and Madrid from Feijóo et al.).

Methods
The sample was obtained from a group of patients with OI, under 18 years of age who attend the Postgraduate Clinic of the Own Title: "Specialist in Integrated Dentistry in Children with Special Needs", from the Faculty of Dentistry of the Complutense University from Madrid (UCM), with the support / funding of a collaboration agreement between Fundación AHUCE and the UCM. A total of 31 patients were studied. The distribution of the final sample consisted of 31 patients 18 children and 13 girls distributed in 10 children/as for types I and IV respectively; and 11 children for type III OI according to the classification of Sillence et al, likewise for the absence / presence of Dentinogenesis imperfecta (DI-I), the distribution was 19 children and 12 children respectively. The patients treated with bisphosphonates in this sample were a total of 16 children distributed according to the number of cycles of zoledronate ≤ 5 cycles that corresponded to a total of 10 children and > 5 cycles a total of 6 children. In all patients, dental age according to Demirjian in the French-Canadian population was determined, as well as dental age according to the Demirjian method using the specific maturation tables for Spanish population proposed by Feijóo et al. This research has been carried out with the support/funding of the AHUCE-UCM Foundation (collaboration agreement).

Results
When analyzing the dental age of the sample it was observed that most of the sample presents an advance of the dental age (the dental age is greater than the chronological age), presenting this advance between 64 and 71% of the patients depending on the reference tables used (Demirjian and Feijóo respectively). There were no statistically significant differences between the maturation tables of the French-Canadian and Spanish populations. Children with OI type III have a more marked advance (> 1 year) (36.4%) than those of type I and IV (30%), as well as the delay (> 1 year) of dental age it was higher for type III (18.2%) compared to 10% for types I and IV. The children with DI-I presented an advance in their dental age (>1 year) more prevalent (50%), than in those who were absent (21.1%). The differences found between the chronological age and dental age related to the treatment with zoledronate show us a tendency to the advance of the dental age.
Children with OI who have received a shorter treatment (≤5 cycles of zoledronate) show a higher frequency (20%) of delay in their dental development, compared to 10% that present advancement. While those who have received a prolonged treatment (> 5 cycles of zoledronate) more often present advancement in their dental development (33.3%).

Conclusions
It was observed that children with OI present a generalized advance of dental age, both with respect to the French-Canadian population studied by Demirjian, and with respect to the population of Madrid. Patients with type III OI had greater alterations regarding the deviation of dental age with respect to chronological age compared to patients with type I and type IV OI. Regarding the administration of bisphosphonates, it was observed that those who received more prolonged cycles (more than 5) presented more frequently the advance of dental age.

O3
Evaluation of the severity of malocclusion in Spanish children affected by osteogenesis imperfecta

Nuría Gallardo López
Master’s Degree in Pediatric Dentistry/Complutense University of Madrid, Madrid, Spain

Co-authors: Fabiola Bernal-Barroso, Joaquín de Nova-García, Montserrat Diéguez-Pérez, Antonia María Caleya-Zambrano

Background
The occlusion is the way the dental arches are related to each other. This is characterized by a balance between the craniofacial growth which is in harmony with the growth of the maxilla and the jaw in terms of size, shape and position. Measure and quantify the malocclusion is essential for a good orthodontic diagnosis but also for epidemiological studies where we can measure the prevalence and the incidence of malocclusion in a certain group of people. Osteogenesis Imperfecta (OI) is a connective tissue disease most commonly involving mutation of the genes that codify type I collagen that affects many organs in the body, especially the skeleton. The Silence classification it divides the disease in four major categories based on clinical, radiographic and genetic criteria.

Patients with OI present unique morphological characteristics as a direct result of the molecular defect they present, leading to a deficit of bone growth and mineralization. The anomalies differ greatly on the type of OI they present. Craniofacial morphology has a wide range of variety from almost normality in type I to severe type III dysmorphism with a typical triangular face, anomalous sagittal relationship, maxillary retruded with respect to the anterior cranial base (SNA Angle decreased) and increase in the SNB Angle. This describes an advanced mandibular position in relation to the anterior cranial base, resulting in true Class III patterns.

Objectives
The main objective of our study was the evaluation of the severity of malocclusion in a group of OI patients in temporary, mixed and adult dentition. The secondary objective was to create a method to analyze the malocclusion in temporary dentition patients, to date not available at these ages; to apply the ABO Discrepancy Index in mixed and adult dentition to evaluate the severity of malocclusion in OI and determine differences between the OI group and the control group; to mention according to the classification of Silence, which types of OI has the more severe malocclusion and finally to find out which are the variables of the index and method that more influence on the complexity of the malocclusion.

Methods
We have analyzed a total of 49 patients (25 females and 24 males) with ages between 4 and 18 years, with different types of OI, distributed in the following percentages: OI type I (n=13); OI type III (n=18); OI type IV (n=8) and OI type V (n=2); 41 of them were in permanent and mixed dentition and 8 of 13 them were in temporary dentition. The control group consisted of 49 patients with no history of disease, matched at the beginning by age and gender and type of malocclusion with the OI group. For each patient we had a complete intra and extraoral photographs and ortopantomography and lateral radiography when possible. We chose the Discrepancy Index for the evaluation of the malocclusion in our group of patients, because it was the one that best suits with our sample. We also use the method created by us for the temporary dentition patients which we called Temporary Analysis Method. All the
results were compared by statistical test. This research has been carried out with the support / funding of the AHUCE-UCM Foundation (collaboration agreement).

Results
Most of the patients of the sample shows Class III malocclusion (61%), followed by Class I (34.1%). No statistically differences were found between the control group and the OI group in the Angle Molar class as we 14 matched both groups at the beginning of the treatment according to the Angle molar class. The total score of the DI shows statistically significant differences between both groups, in the control group the results shows a moderate-low difficulty of treatment whereas in the OI group the score shows a high difficulty. In the lateral open bites, we found statistically significant differences at the 95% (p= 0,002 en la T de Student and Mann-Whitney p=0,001), in the OI group the incidence is very high where as in the control group is rare to find it. The variable others which involves agenesias, ectopic eruption, deviations from the middle line more than 3 mm shows statistically significant differences at 95% (p= 0,004 en la T de Student y Mann-Whitney p=0,001) between the control group (0,44) and the OI group (1,93). In the OI temporary dentition group, no significant differences were found in any of the variables studied by the Analysis Method between the control group and the OI group.

Conclusions
OI patients present more severe of malocclusion compared with a control group with no disease; the severity of malocclusion increase as the degree of severity of the disease increases, so type III and IV has more difficulty of orthodontic treatment than type I and finally the variable of the DI that most affect the severity of malocclusion are lateral open bites and "others" which implies agenesia, ectopic eruption and deviation of the middle line.

Background
The dental eruption is a physiologic process that confirms the normal development of children. It can be affected by several local and systemic disturbances, and there are a number of diseases that have been related to eruptive disturbances in children. The Osteogenesis Imperfecta (OI) presents with a major skeletal involvement, with oral effects, related to disturbances in dental development (E.g. Dentinogenesis Imperfecta, malocclusions and dental impactation). The treatment guidelines advise the use of drugs, which modify the bone remodelling (bisphosphonates), these may condition the physiologic eruptive process in the children affected. Recent and scarce studies report, that although the disease itself does not affect the eruptive process, this can be slowed down in those children on bisphosphonates.

Objectives
The general aim of the project was to study the dental eruption chronology in deciduous and permanent dentition in children affected by different types of Osteogenesis Imperfecta receiving bisphosphonates. The specific objectives were: to state the chronology and pattern of eruption in deciduous and permanent teeth in a sample of OI children; to study the chronology differences between arch, side and gender; to analyse these disparities according to the type of OI and the bisphosphonates’ treatment, to compare the eruption chronology in OI children with a control sample of healthy children.

Methods
Study sample: 44 children and adolescents aged between 5 to 15 years old, 14 children aged between 3 and 41 months. Parent Consent was obtained for all of them as well as approval from the children. An erupted tooth was considered as
such when the tooth had penetrated the oral mucosae and it was visible in the oral cavity. The data abstract 22 gathering regarding the teeth eruption was collected using: intraoral exam by a Dentist (main source); questionnaire sent to parents; and exam by a Paediatrician. A Paediatrician recorded all the information about their treatment in the medical notes. The control sample was obtained from previous studies done on large a population of healthy children. This research has been carried out with the support/funding of the AHUCE-UCM Foundation (collaboration agreement).

Results
The mean age for eruption on each tooth as well as its eruptive pattern were obtained. A delay on the eruptive age for permanent and deciduous teeth was observed when comparing it with the control sample, with a range that went from a maximum of 2.5 years on the 3.1 tooth (lower left central permanent incisor) and a minimum of 2.2 months in the 3.5 tooth (lower left second premolar) in permanent dentition. In deciduous dentition the range went from 13.84 months in the 8.1 tooth (lower right deciduous central incisor) to a minimum of 0.93 months in the 5.5 tooth (upper right second deciduous molar). The differences with the control sample showed to be statistically significant, except for the first upper premolars and the second lower premolars in permanent dentition. In deciduous dentition, the right canine, the second upper molars and the lower left second incisor and canine did not show significant differences either. In the control sample, the right and left lower second deciduous molars emerge later (0.27 months for the 8.5 tooth (lower right second deciduous molar) and 0.03 months for the 7.5 (lower left second deciduous molar) than on the OI children, although no significant evidence for this. The eruption pattern in permanent and deciduous teeth from OI children were similar to the control sample; except for the deciduous canines which erupted before than the first molars in deciduous dentition in children with OI.

Conclusions
In this study, children with Osteogenesis Imperfecta treated with bisphosphonates had a delayed eruption of deciduous and permanent dentition when comparing it with the control sample. The treatment with bisphosphonates may then affect the physiological eruptive process. The aforementioned should be controlled so the Paediatrician could tailor the drug dose accordingly.

O5
An audit of the referral pathway for OI patients between Great Ormond Street Hospital and the Eastman Dental Hospital
Armaana Ahmad
Paediatric Dentistry, Eastman Dental Hospital, UCLH, London, United Kingdom
Co-authors: Dr Susan Parekh, Dr Belinda Crowe, Dr Catherine DeVile

Background
Children with Osteogenesis Imperfecta (OI) are recommended to have a dental assessment within 6 months of eruption of the first baby teeth (Brittle Bone Society, UK). Children seen in the OI service at Great Ormond Street Hospital (GOSH) should be routinely referred for dental assessment to the Paediatric Dentistry department at the Eastman Dental Hospital (EDH). The outcome of this assessment should be communicated back to the OI team.

Objectives
To ensure children with OI referred to EDH are receiving specialist dental assessments, and the outcome of these assessments are being reported back to the OI Clinic team at GOSH.

Method
Audit of the referral pathway of patients referred to EDH to assess the following standards:
• All OI patients referred to EDH should have a specialist dental assessment
• All OI patients attending an appointment at the Paediatric Dentistry Department, should have a letter summarising the findings sent to the OI team
• EDH should communicate the outcome of all referrals to the OI team, including cases of non-attendance GOSH maintains a database of patients referred to EDH. Patients who should have been referred in 2017 and 2018 were identified and a search of the EDH electronic patient records identified those who had referrals registered. The outcome of their referral, appointment history,
correspondence and dental diagnoses were recorded from the patient records.

Results

The OI clinic at GOSH sent 81 referrals to the EDH in 2017 and 2018; EDH registered referrals for 65/81 (80%) of these patients.

- Of the 65 referrals registered: ~20 (31%) children were not given appointments, none had records of letters sent to the OI team.
- ~39 patients attended appointments; 31/39 (80%) had letters sent to the OI team, 5/39 (13%) had letters sent to health care professionals without copying to the OI team, 3/39 (8%) had no letters sent.
- ~3 patients cancelled their appointments, 2 had letters sent to the OI team.
- ~3 children were not brought to their appointments, 2 had letters sent to the OI team.

- Of the 39 patients seen for dental assessment: ~26 (67%) were male, 16 (41%) were aged under 7 years and 7 (18%) had previously attended EDH.
- ~20 (51%) attended follow up specialist paediatric dental appointments.
- ~3 patients attended for joint specialist orthodontic and paediatric care.
- ~16 (41%) were discharged for care with a general dental practitioner.

- The following dental diagnoses were made: 11 (28%) Active dental caries, 4 (10%) Dentinogenesis Imperfecta, 5 (13%) Anomalies of enamel mineralisation, 4 (10%) Dental Trauma, 6 (15%) Malocclusions, 4 (10%) Impacted teeth, 3 (8%) Ectopic teeth, 4 (10%) Hypodontia, 2 (5%) Microdontia, 4 (10%) Other dental diagnoses and 13 (33%) No evidence of dental anomaly or disease.

The standards were not met:

1. Only 39/81 (48%) of OI patients referred by GOSH had a specialist dental assessment.
2. 31/39 (80%) patients attending for specialist assessment had letters sent to the OI team.
3. 30/65 (46%) of referrals registered by the EDH, had no evidence of letters indicating the outcome of the referrals sent to the OI team.

Discussion

There was a disparity between the GOSH record of referrals sent and referrals registered at EDH, as this audit focused on the EDH referral pathway an audit of the GOSH referral pathway is recommended. During the audit period, referrals were sent by post or fax. The introduction of a common email domain (nhs.net), allowing electronic referrals which can be clearly tracked, will hopefully improve the process for referrals. The low proportion of patients being given appointments after referral may be explained by patients being sent a letter to contact for an appointment, instead of an appointment date, which may have resulted in parents not appreciating they needed to contact the hospital. Since the audit, patients are now sent appointments. A new electronic patient record system should simplify this process and will be fully auditable. The range of dental issues noted in children assessed demonstrates the need for all children with OI to have access to dental care, and assessment by specialist dental services.

Actions points

1. Dissemination of audit results through presentation to staff.
2. Reminder to address letters to referrers or CC to OI team.
3. Reminder for procedures for failed appointments including letter writing responsibility.
4. A list of patients who have not been seen at EDH sent to OI team administrator to assess if re referral is required.
5. Review of the correspondence processes for referrals received to EDH.

Conclusions

The introduction of NHS email and a new electronic patient record system integrating referrals, triage and patient notes across both sites provides an opportunity to improve the referral pathway and communication between teams at GOSH and EDH. A second cycle audit is required to see if the referral pathway improves.
**Background**
Children with Osteogenesis Imperfecta (OI) can have significant dental concerns, including Dentinogenesis Imperfecta (DI) and malocclusion. To promote excellence in dental care provision to the paediatric OI population, a referral pathway exists between the Highly Specialised OI Regional Centre at Great Ormond Street Hospital (GOSH) and the Paediatric Dental team at the Eastman Dental Hospital (EDH).

**Objectives**
1. To audit patient access to dental healthcare, both local and specialist
2. To identify the prevalence of patient concerns about their dentition, with specific reference to four areas of concern: ‘appearance’, ‘bite’, ‘pain in the teeth’ and ‘pain in the jaws’.

**Method**
From October to December 2018, during routine OI clinic reviews, five standard questions were asked to patients and/or their families by an attending dental researcher, and answers recorded manually on a questionnaire. With one exception (due to ongoing investigations around non-accidental injury precluding the researcher attendance in clinic) all attending families were approached. No age restrictions to participation were applied.

**Analysis**
Data was collated and simple analysis achieved using Excel.

**Results**
In total, 86 children and families participated [49 male (57%) and 57 female (43%)], with an age range from 2 months to 18 years. Of these, 9 (10%) were new to the OI service and 77 (90%) were follow-up patients. Overall: - 78 (91%) children were receiving some form of dental care. Of these, 49 (57%) children were under the care of a local dentist only, 6 (7%) children were under the care of the EDH only, and 23 (27%) children were under the care of both the EDH and a local dentist. Of the 8 (9%) children who were not receiving any dental care, 7 were aged between 2 months to 3 years old and 1 was 16 years. - 8 (9%) children reported problems accessing appropriate dental care; 3 from the local dentist, 3 from the orthodontist, and 2 from the EDH. - 37 (43%) children and families reported no dental concerns and 49 (57%) participants reported one or more dental concerns [30 (35%) reported one concern, 19 (22%) reported multiple concerns]. Of the 57 (66%) children not referred to the EDH for specialist review by child/family report, 34 (60%) had at least one type of concern. Participants were then divided by age into 3 groups: 27 (31%) were classified as primary dentition (<6 years old), 41 (48%) as mixed dentition (6-12 years old) and 18 (21%) as permanent dentition (>12 years old).

**Overall:** - The mixed dentition group reported the greatest concerns across the assessed areas, with the exception of ‘pain in the jaws’ which was most prevalent in the permanent dentition group. - 27/41 (66%) of the mixed dentition group reported at least one type of concern. Their most frequent concern was ‘appearance’ [18/41 (44%)], followed by ‘pain in the teeth’ [11/41 (26%)] and ‘bite’ [9/41 (22%)]. Pain in the jaws was reported by only 1 child.

**Conclusions**
This audit has highlighted dental concerns in children with OI and the importance of ongoing access to dental care to address concerns.

1. Whilst overall access to dental healthcare was good, access to specialist dental care was unsatisfactory at 29 (34%). Less than half of participants reported receiving a referral to the EDH despite a clear referral pathway in place. Of these, 60% of these had at least one current dental concern,
highlighting a high level of unmet needs in those not accessing specialist services. Action: The referral pathway to the EDH must be reviewed to ensure every child with OI is offered a specialist review appointment and that dental referrals made by the OI team are received and actioned by the EDH.

2. Concerns about dentition are common within OI, with 49 (57%) participants reporting current dental concerns. Children in the mixed dentition years appear particularly vulnerable to dental concerns.

Action
The referral pathway needs to be reviewed to ensure children are seen by specialist dentists, who can identify and manage dental concerns in children in OI. Specialist review might best be timed to fall within the mixed dentition stage of development. Additional finding: Of the 8 children identified as not receiving any dental care, it is likely 7 were considered by their parents as being too young to receive dental care. Parents are currently advised by the OI team to seek local dental care for their children once primary dentition starts to appear. This practice should continue, to ensure good habits are established around dental care and provide opportunity for DI to be picked up early.

**P2**

**Study of the craniovertebral junction in the osteogenesis imperfecta patient**

Nuria Gallardo-López
Master’s Degree In Pediatric Dentistry/Complutense University of Madrid, Madrid, Spain
Co-authors: Mercedes Ríos-Rodenas, Joaquín de Nova-García, Rafael García-Sola, Marta Paz-Cortés, Ana Bueno-Sánchez

**Background**
Osteogenesis imperfecta (OI) is a genetic disorder of connective tissue that causes increased bone fragility and low bone mass. Patients suffering OI usually present dental anomalies and important occlusal problems. For this reason, it is normal to perform lateral skull radiographs for the orthodontic diagnosis of these patients. With this diagnosis image, the dentist should analyse the junctional area between skull base and spine, which could be damaged in OI. Craniovertebral junction (CVJ) abnormalities are one of the most important complication of OI. The reason for the development of skull base abnormalities in OI is still unknown; however, it is believed that the deformation of the skull is caused by a softness of the skull or by to repetitive microfractures in the region of the foramen Magnum.

**Objectives**
The primary objectives was to evaluate the CVJ in children with OI, under bisphosphonate treatment, in lateral skull radiographs and midsagittal magnetic resonance imaging (MRI), with standard reference measurements.

**Methods**
19 lateral skull radiographs and 14 MRI of 28 OI patients were analyzed (age range: 6-18 years old). Our cephalometric method of the CVJ included 8 lineal measurements (McRae, Chamberlain, McGregor modificada, Kovero, Wackenheim, Ranawat, Ranawat modificada, Redlund-Johnell) and 5 angular measurements (Arponen, craneovertebral, clivus-canal, basal y Boogard). We compared our results with 38 lateral skull radiographs and 28 MRI of age-matched healthy patients. This research has been carried out with the support / funding of the AHUCE-UCM Foundation (collaboration agreement).

**Results**
Comparative analysis of the groups: There are changes at the skull base in growing individuals that could be associated with age. Ranawat’s line, Ranawat modified’s line and Redlund-Johnell method have a positive correlation with the age and anterior cranial base angle has a negative correlation. The processus odontoideus of the axis in severe OI patients is closer to the skull base than in mild OI patients. In the same way, the anterior skull base is flattened in severe OI patients more than moderate and mild OI patients. The measurements of the CVJ in OI patients are abnormal when we compared with controls age-matched. Statistically significant difference was detected in the line of McRae, Chamberlain, Wackenheim, Ranawat, Ranawat modified, Redlund-Johnell and in the angles of Arponen, craneovertebral, clivuscanal and basal. The differences were located between the control group and the severe forms of OI. CVJ
abnormalities in OI children: arranged into three groups. Basilar invagination is a protrusion of the odontoid process into the foramen Magnum. The obtained results above 0 for the McRae measurement were considered abnormal. Three out of our 28 OI patients have this criteria (10,7%). Basilar impression takes place when the position of the odontoid process is significantly above the caudal borders of the skull, without penetrating in the interior of the foramen Magnum. To diagnose Basilar impression, we considered ten measurements, 7 lineal and 3 angular. The radiographic criteria for basilar impressions is fulfilled if these measurements are ±2,5 SDs above the average of age-matched healthy controls. The results obtained showed that 10 patients (35,7%) had this anomaly. Platybasia is a flattening of the anterior cranial base. It is diagnosed when the anterior cranial base angle or the Boogard’s angle was more than 2,5 SDs above the average of healthy controls. Platybasia was the most prevalent diagnosis (39,3%). Patients who had at least one of these diagnoses were considered to have a skull base anomaly. Overall, 17 (60,7%) of the 28 OI patients exhibited a cranial base anomaly.

Conclusions
The processus odontoideus of the axis in OI patients is closer to the skull base than in control patients. Also, the anterior skull base is flattened in these patients. This probable pathology is more important in severe forms of OI (types III and IV). From a sample of 28 patients with OI, 17 (60,71%) have at least a cranial base anomaly, considering the 2,5 DS limit, if we compare their values with the healthy control age-matched values. Overall, 3 patients (10,71%), have basilar invagination, 10 patients (35,71%) have basilar impression and 11 patients (39,29%) suffer from platybasia. The lateral skull radiograph and the standard measurements estimated, provide us a good early diagnosis image to anticipate abnormalities in the CVJ of these patients.

P3
Morphological study of the dental structure with electronic scanning microscopy in a Spanish sample of patients with osteogenesis imperfecta
Andrea Martin-Vacas
Paediatric Dentistry, Universidad Complutense de Madrid (UCM), Madrid, Spain
Co-authors: Joaquin de Novo-Garcia, Vicente Vera-Gonzalez, Rosa Mourelle-Martinez, Belén Sagastiabal-Cardelús

Background
Dentinogenesis Imperfecta (DGI) is a hereditary condition of dentin that is associated with Osteogenesis Imperfecta (OI). The alteration of the metabolism of type I collagen, mainly at the level of the COL1A1 and COL1A2 genes, gives rise to anomalies in the dental structure, which is manifested by clinical and radiographic dental alterations. Although scientific advances have allowed a better knowledge of the disease, it’s necessary a protocolized study that analyses the ultrastructural anomalies, providing an adequate definition of the DGI-I.

Objectives
The general objective of the research was to study and describe the involvement of the temporal dentition of subjects with OI at the enamel, dentin and dentin-enamel junction by means of scanning electron microscopy, in comparison with an unaffected control group. In addition, we proposed to compare, both with the control group and between the OI phenotypes, the tubular diameter, the tubular count, and the amount of calcium and phosphorus in the dentin. Subsequently, the relationship between the ultrastructural findings and the presence of alterations at a clinical and radiographic level was analysed.

Methods
The enamel, the dentin-enamel junction and four points of the dentin of 25 temporary teeth from patients with OI and 30 control teeth were analysed by scanning electron microscopy. Subsequently, the clinical and radiographic alterations of subjects with OI were analysed, in relation to the dental ultrastructural findings. Statistical tests were performed with a confidence level of 95%. This work has been carried out with
the support and financing of the collaboration agreement Fundación AHUCE-UCM.

Results
Structural alterations were observed in enamel (60%), dentin-enamel junction (64-72%) and dentine (100%) in teeth of subjects with OI, with occlusal dentin being more frequent and severe in subjects with a most serious phenotype of OI (p < 0.012). The tubular density in teeth with OI is lower in pulp dentin compared to control teeth (p 0.027), in addition to a greater density and tubular diameter in the occlusal dentin region (p 0.003 and p 0.018), significant differences being found (p <0.05) between OI type I (mild) and type III (severe). The amount of dentin calcium is similar in the teeth with OI to the control group (p 0.478), but a lower amount of phosphorus is found (p 0.016), although there are no differences (p> 0.05) with respect to the phenotype of the OI. The subjects with OI presented clinical (41.2%) and radiographic (69.2%) alterations, being the clinical alterations more frequent in the most severe OI phenotypes (p 0.044). A 30.8% of the sample did not present clinical or radiographic alterations, while 38.5% had isolated radiographic alterations and 30.8% combined clinical and radiographic alterations, although without statistical significance.

Conclusions
The subjects with OI present ultrastructural dental alterations in the enamel, dentin-enamel junction and dentine. There are differences in dentinal tubular diameter and density between the teeth with OI and the controls in the pulp and occlusal dentin, finding differences between type I and III of OI. The teeth with OI have a lower amount of phosphorus than the control teeth. Patients with OI present clinical and radiographic dental alterations defined as DGI-I. The clinical-radiographic alterations may be absent, presented exclusively radiographic or appear simultaneously at both levels.
Sponsors & supporters

Supporters

Silver sponsor

Alexion
www.alexion.com

Alexion Pharmaceuticals, Inc. is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare diseases including hypophosphatasia (HPP).

Other supporters

Mereo Biopharma
www.mereobiopharma.com

Mereo is a UK-based international biopharmaceutical company focused on developing innovative treatments in the field of rare diseases; and to bringing these to patients in a timely and sustainable way. Our mission is focused on providing new therapies to patients with chronically debilitating life-limiting rare diseases that have few, if any, other treatment options.

Exhibitor

Cast Print

Find out more: http://castprint.co/
Practical information
PRACTICAL INFORMATION FOR PARTICIPANTS

Attendance Certificates
Attendance certificates (PDF-versions) are available on request to office@oife.org after the conference.

Food and beverage
The following meals are included in the conference fee:
- All coffee & refreshment breaks
- Buffet lunch Friday & grab & Go lunch on Saturday
- Welcome Reception & Conference dinner on Friday

Name badges
Please wear your name badge at all times when you are in the conference area/hotel.

Photography/Recording
You are respectfully requested not to take photos or recordings during sessions.

We will have a professional photographer hired by the company Mereo Biopharma taking photos during the breaks and meals. Photos will be used in communication material of Mereo Biopharma and/or OIFE and our member organizations. We have asked consent in the registration form. If you have questions on this - please ask at the registration desk.

Registration desk & slide reception opening times
Thursday June 13th: 18.00 - 21.00
Friday June 14th: 08.00 - 09.30
Saturday June 15th: 08.00 - 09.30

Valuables
You are reminded that you are responsible for your valuables and you should take care not to leave them unattended at any time.

Wi-Fi
There is free Wi-Fi in the whole conference area.