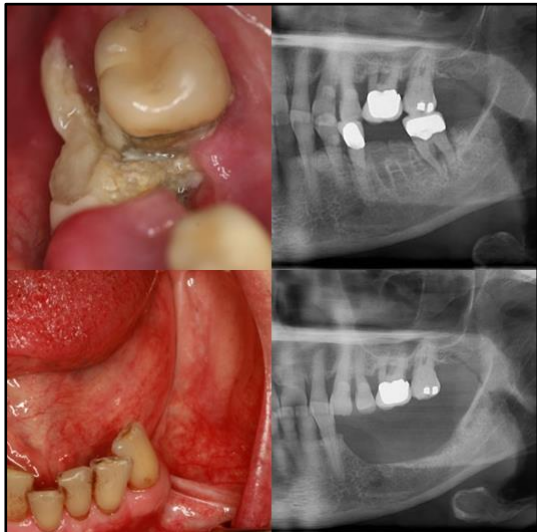
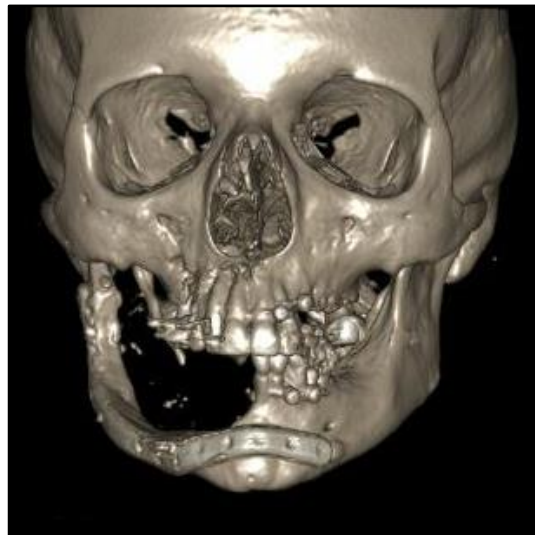


2nd INTERNATIONAL SYMPOSIUM ON MEDICATION RELATED OSTEONECROSIS OF THE JAWS (MRONJ) IN COPENHAGEN

2nd of November 2018



For further information please see our website: www.rigshospitalet.dk/MRONJ

Supported by Amgen



2nd INTERNATIONAL SYMPOSIUM ON MEDICATION RELATED OSTEONECROSIS OF THE JAWS (MRONJ) IN COPENHAGEN

Introduction

Medication Related OsteoNecrosis of the Jaws (MRONJ) is a serious complication to antiresorptive treatment meant to reduce unwanted skeletal events for cancer and osteoporosis patients. MRONJ can lead to pain in the jaw, loss of teeth and jaw bone, impaired chewing function, and thereby loss of quality of life.

Following the First International Symposium held in Copenhagen in 2017, we have invited ten European experts, who will update You on the latest scientific results. The speakers are highly recognized clinicians and scientists from Germany, Italy, England, Greece, Switzerland, Norway and Denmark. The target audience are private practitioner dentists, clinicians and maxillofacial surgeons and other specialists. There is a constant need for update on diagnosis, treatment and especially prevention, which we will address in order to help the numerous MRONJ patients in Europe.

PLACE OF SYMPOSIUM

LOCATION: Center For Leadership (CFL)

ADDRESS: Folke Bernadottes Allé 45
2100 Copenhagen
Denmark



INFORMATION ON REGISTRATION AND PAYMENT

CHAIRMAN: Morten Schiodt

CONTACT PERSON: Line Lund Eriksen

TELEPHONE: +45 3545 5181. Monday-Thursday 07.30-14.30.

WEBSITE: www.rigshospitalet.dk/MRONJ

EMAIL: 2ndCopenhagenMRONJsymposium.rigshospitalet@regionh.dk

PRICE: Dentists / Doctors / Others: 140 EURO / 1050 DKK.
Students / Trainees: 90 EURO / 650 DKK



SYMPOSIUM PROGRAM

Friday November 2, 2018 8.30-17.00

8.30-9.00: *Breakfast*

9.00-9.15 **Morten Schiodt, Chairman, Copenhagen:**

Welcome, introduction and follow-up from first Symposium in 2017.

9.15-9.30 **Stefano Fedele, London:**

What is MRONJ?

Definition, classification, epidemiology, trends.

9.30-9:45 **Sven Otto, Munich:**

Clinical manifestations of MRONJ.

9.45-10.00 **Sven Otto, Munich:**

What is the evidence for infection as a risk factor for MRONJ?

(including summary of other risk factors)

10.00-10.20 **Roman Guggenberger, Zurich:**

Imaging of MRONJ

- a. Radiologic features
- b. Cone Beam Tomography, CT Scan
- c. Scintigraphy
- d. MR

10.20-10.45: Coffee Break

10.45-11.00 **Sven Otto, Munich:**

Treatment of MRONJ - 1:

Indications and procedures for minimally invasive surgery for MRONJ

11.00-11.15 **Morten Schiodt, Copenhagen:**

Treatment of MRONJ - 2:

Indications and procedures for block resections and use of buccal fat pad for closure of maxillary defects

11.15-11.30 Thomas Kofod, Copenhagen:

Treatment of MRONJ - 3:

Indications and procedures for continuity resections and major reconstructive surgery of MRONJ, including use of Computer assisted 3D planning.

11.30-11.45 Alberto Bedogni, Padova:

Treatment of MRONJ - 4:

Results of surgical management of MRONJ based on a clinic-radiological classification system. An 8-year cohort.

11.45-12.00 Bente Brokstad Herlofson, Oslo:

Treatment of MRONJ - 5:

When to treat non-surgically (conservative treatment).

Ethical and other dilemmas.

12.00-12.15 Summary and questions from the audience.**12.15-13.00: Lunch**

13.00-13.15 Ourania Nicolatou-Galitis, Athens:

Periodontal disease and MRONJ.

How to distinguish between periodontal disease and MRONJ affecting the periodontal tissues?

13.15-13.30 Stefano Fedele, London:

Exposed and non-exposed MRONJ.

How do we distinguish between apical periodontitis with periapical fistula and MRONJ?

13.30-13.40 Morten Schiodt, Copenhagen:

Tooth extraction in patients on Antiresorptive treatment.

Can we control the risk of MRONJ?

13.40-13.50 Camilla Ottesen, Copenhagen:

Drug holiday: Should the antiresorptive treatment be paused or stopped when MRONJ is diagnosed? - or when tooth extraction is needed?

13.50-14.00 Alberto Bedogni, Padova:

Tyrosine Kinase Inhibitors and other new drugs: What is their role in MRONJ?

14.00-14.10 Sanne Werner Møller Andersen, Copenhagen:

Is Rehabilitation of MRONJ patients with Dental Implants possible?

14.10-14.30: *Coffee break*

14.30 -16.00 Cases to solve for the participants – group work at the tables.

16.00-16.10 Ourania Nicolatou-Galitis, Athens:

Prevention of MRONJ.

16.10-16.20 Ourania Nicolatou-Galitis, Athens:

Education of health care providers and patients.

16.20-16.55 Round table discussion

Moderator: Morten Schiødt

Sven Otto, Alberto Bedogni, Ourania Nicolatou-Galitis, Stefano Fedele, Roman Guggenberger, Bente Brokstad Herlofson and Thomas Kofod.

Questions from the audience

16.55-17.00 Morten Schiødt:

Summary and Closing the Symposium.

Presentation of symposium speakers

To be held in Copenhagen, Denmark on the 2nd of November 2018



Alberto Bedogni

Curriculum Vitae, Alberto Bedogni. University of Padova, Italy.

Dr. Alberto Bedogni is Director of the Regional Center for Prevention, Diagnosis and Treatment of Medication and Radiation-related Bone Diseases of the Head and Neck since 2014. He is Assistant professor of Maxillofacial Surgery at the Department of Neurosciences-DNS, University of Padua, and Consultant at the Unit of Maxillofacial Surgery, Hospital Trust of Padua. His basic and clinical research focuses upon osteonecrosis of the jaws, bio-molecular markers in head & neck cancer, peripheral nerve regeneration, regenerative medicine and development of CAD-CAM customized titanium prototypes for jawbone reconstruction. He is coordinator of the Expert Panel Committee of the Italian Societies of Maxillofacial Surgery (SICMF) and Oral Medicine and Pathology (SIPMO) and is co-author of the Italian Recommendations for the prevention, diagnosis and treatment of MRONJ published in 2013. He also actively contributed to the preparation of the guidelines on prevention of bisphosphonate-related ONJ in the cancer population, on behalf of the Italian Ministry of Health (2014). He has been coordinator of a research team who published several clinical papers in the last 10 years on the prevention, treatment and pathogenesis of BRONJ and few of the very initial reports on bevacizumab and sunitinib-related ONJ. He contributed to develop an international network of clinical research centres and promoted several multicentre studies on MRONJ.



Stefano Fedele

Curriculum Vitae, Stefano Fedele. University College London, Eastman Dental Institute, London, England.

Professor Stefano Fedele is Head of Department of Clinical Research and Full Professor of Oral Medicine at University College London, Eastman Dental Institute. His research activities focus upon clinical and translational research in Oral Medicine with a special interest in MRONJ. Through international collaboration he set up a network of centers collecting clinical data and DNA of a cohort of MRONJ patients and drug-exposed controls to inform clinical and pharmacogenetic (genetic predisposition) studies. He has led a team of international investigators to publish a number of research papers on the non-exposed variant of MORNJ, which led to the revision of MORNJ definition by the AAOMS. Twenty-eight sites from seven countries have contributed to his Genome Wide Association study (GWAs), which over the last 7 years has collected DNA from ~1,000 MRONJ patients and has identified, for the first time, a genetic variant significantly associated with the risk of MORNJ development.



Roman Guggenberger

Curriculum Vitae, Roman Guggenberger. University of Zurich, Switzerland.

Dr. Roman Guggenberger was born in Innsbruck, Austria where he studied medicine at the Medical University. After training and obtaining full license as a general practitioner in Austria, he moved to Zürich, Switzerland and finished his training in general radiology at the Department of Diagnostic and Interventional Radiology. He was fellow at the radiology department of the Orthopedic University Hospital in Zürich and subspecialized in musculoskeletal radiology and also performed a fellowship in pediatric neuroradiology at the Children`s Hospital in Zürich. He has obtained the Swiss diploma of diagnostic neuroradiology and became associate professor in 2016. Dr. Guggenberger is now a senior staff member and head of the musculoskeletal radiology imaging and research group at the Department of Diagnostic and Interventional Radiology in Zürich. He has spent most of this research career in evaluation and optimization of different imaging techniques for diseases of the musculoskeletal system. A strong focus of his work is on cone-beam CT in its various forms and peripheral nerve imaging. He has also published several works on bisphosphonate-induced osteonecrosis of the jaw and its detectability in different imaging techniques.



Ourania Nicolatou-Galitis

Curriculum Vitae, Ourania Nicolatou-Galitis. University of Athens, Greece.

Ourania Nicolatou-Galitis, DDS, MSc, DrDEnt, Ourania Nicolatou-Galitis, www.nicolatou-galitis.com, www.dentaloncology.gr, www.dentaloncology.eu.

Oral Medicine, Oral Oncologist, Professor of the National and Kapodistrian University of Athens, Dental Oncology Unit, Dental School, dent.uoa.gr.

Dr Ourania Nicolatou-Galitis graduated from the Dental School of the National and Kapodistrian University of Athens. She obtained her Master's Degree and Certificate in Oral Pathology from Temple University, Philadelphia, USA.

Current positions:

- Professor and Head, Clinic of Hospital Dentistry, 2010-present
- Responsible of the Graduate Program in Hospital Dentistry, 2010-present
- Founding member and President of the Hellenic Society of Oral Oncology, oraloncology.gr, 2005-present
- Founding member and member of the Board of the Hellenic Society of Head and Neck Cancer, headneckcancer.gr, 2016-present
- Past President of the International Society of Oral Oncology-ISOO, 2017-2019
- MASCC Strategic Planning Committee, mascc.org, 2017-2020
- Chair of the Bone Study Group, mascc.org, 2015-2020

Osteonecrosis of the jaw in medication is currently the main clinical and research focus of Dr Ourania Nicolatou-Galitis.

She serves as a referral center for many Cancer Centers of Greece.

She is the principal investigator for the AMGEN Registry Study for osteonecrosis in the Athens Dental School Center.

As Chair of the Bone Study Group of MASCC, she has initiated a systematic review on the specific clinical questions (1) «to do or not to do the dental extraction» when a cancer patient receives medications related to osteonecrosis and (2) how to treat, when osteonecrosis develops.



Sven Otto

Curriculum Vitae, Sven Otto. Ludwig-Maximilians-University of Munich, Germany.

PD Dr. med. Dr. med. dent. Sven Otto has dealt intensively with clinical presentation, pathogenesis, prevention and treatment of medication-related osteonecrosis of the jaw. He has developed a pathogenesis theory putting infection and infection associated pH changes in the centre of the focus and collected cell cultural and clinical evidence for this hypothesis. He has also contributed to the clinical implementation of fluorescence-guided surgery for the treatment of MRONJ. Together with the AO research institute in Davos a minipig large animal model for MRONJ was established which could contribute to the further understanding of MRONJ. Together with Springer publishing he has edited the textbook "Medication-related osteonecrosis of the jaw: Bisphosphonates, Denosumab and New Agents".

1997-2006 Dental and medical studies at the university of Leipzig (Germany)

2006-2012: Specialty training for Oral and Maxillofacial Surgery, LMU München

seit 05/2012: Board examination for Oral and Maxillofacial Surgery, LMU of Munich

2013: Habilitation dealing with „Bisphosphonate-related osteonecrosis of the jaw“

since 2013 Senior Consultant of the department of Oral and Maxillofacial Surgery of Ludwig-Maximilians-University of Munich (Head: Professor Dr. Dr. Michael Ehrenfeld)

2014 Editor: Medication-Related Osteonecrosis of the Jaw: Bisphosphonates, Denosumab and New Agents“ (published by Springer)

2015 Scientific Award of the German Association of Oral and Maxillofacial Surgery: „From cell culture over the large animal towards optimization of the prophylaxis and treatment of medication-related osteonecrosis of the jaw“



Bente Brokstad Herlofson

Curriculum Vitae, Bente Brokstad Herlofson. University of Oslo and Oslo University Hospital, Norway.

Professor, specialist in oral and maxillofacial surgery at the Department of Oral Surgery and Oral Medicine, Faculty of Dentistry, University of Oslo and at the Department of Otorhinolaryngology – Head and Neck Surgery Division for Head, Neck and Reconstructive Surgery, Oslo University, University Hospital, Norway. Participating scientist in the Scandinavian ONJ-cohort study, being the Principle investigator in Norway for the establishment of the Norwegian database for the enrolment of all ONJ cases related to antiresorptive treatment during 2011 until 2019. Contributed to the AO Foundation, AOCMF (Switzerland) booklet; Antiresorptive drug-related osteonecrosis of the jaw (ARONJ) – a guide to research, chapter 2; Clinical features of antiresorptive drug-induced osteonecrosis of the jaw, 2016.

Specific research interests: oral morbidity in cancer and cancer treatment, oral oncology, effects of anti-resorptive medication on bone and bone cells, osteonecrosis of the jaw, oral health related quality of life in cancer patient, oral late effects in patients treated for head- and neck cancer.



Sanne Werner Møller Andersen

Curriculum Vitae, Sanne Werner Møller Andersen. Rigshospitalet, Copenhagen University Hospital, Denmark.

Resident in Oral & Maxillofacial surgery at the Department of Oral & Maxillofacial Surgery, Rigshospitalet, Denmark.

Sanne has been part of the Copenhagen research team on MRONJ since 2014. She is now doing a feasibility study investigating rehabilitation of patients on high dose antiresorptive treatment or previous MRONJ with dental implants. Likewise she is investigating the possibility of apicoectomy due to apical periodontitis. Sanne has participated in the multicenter genome study by Stefano Fedele, collecting DNA samples from MRONJ patients in Copenhagen.



Camilla Ottesen

Curriculum Vitae, Camilla Ottesen. Rigshospitalet, Copenhagen University Hospital, Denmark.

Dr. Camilla Ottesen is a PhD student at the Department of Oral Rehabilitation, Faculty of Health & Science at Copenhagen University and at the Department of Oral & Maxillofacial Surgery, Rigshospitalet (Copenhagen University Hospital) supervised by Professor Klaus Gotfredsen and Dr. Morten Schiødt. Camilla has been part of the Copenhagen research team on MRONJ since 2014. She has written a protocol for a randomized controlled trial investigating the importance of drug holiday in cancer patients on high dose antiresorptive medication, in relation to tooth extraction. Camilla is the main investigator of this drug holiday study. Furthermore, she is collaborator in another study of rehabilitation with dental implants in patients on high dose antiresorptive medication or with previous MRONJ.



Thomas Kofod

Curriculum Vitae, Thomas Kofod. Rigshospitalet, Copenhagen University Hospital, Denmark.

Dr Thomas Kofod is Head of Department of Oral and Maxillofacial Surgery at Rigshospitalet (Copenhagen University Hospital). His clinical and research activities focus upon corrective and reconstructive craniofacial and maxillofacial surgery including computer assisted surgery. In MRONJ especially computer assisted resection and reconstruction has been the focus of interest. In close collaboration with Morten Schiødt he parts the Copenhagen research team on MRONJ.



Morten Schiødt

Curriculum Vitae, Morten Schiødt. Rigshospitalet, Copenhagen University Hospital, Denmark.

Morten Schiødt is Senior Consultant, DDS, Dr. odont, and Visiting Professor in Department of Clinical Epidemiology, Aarhus University Hospital.

Specialist Degree in Oral & Maxillofacial Surgery, Copenhagen (Rigshospitalet), Denmark, in 1979.

Doctoral thesis on Oral Manifestations of Lupus Erythematosus in 1984. Teaching and organized symposia in 25 countries. Research on Sjogren's Syndrome, HIV/AIDS, and on Osteonecrosis of the jaws from antiresorptive treatment.

Chairman of the Department of Oral & Maxillofacial Surgery, Cph. Univ. Hospital 2001-2011.

President of the Danish Association Oral & Maxillofacial Surgery for 6 years (1984-86 and 89-91),

President of the Danish Society of Oral & Maxillofacial Surgery for 6 years (1996-2002),

Assoc. Prof. University of California, San Francisco, USA, 1986-1989.

Scientific reviewer 13 international Journals.

Director of SICCA-Denmark founded in 2003, part of NIH-funded multicenter project leading to new classification of Sjogren's Syndrome. NIH funding 12.5 mill \$. Author or co-author of 186 publications.

Present positions:

2003 – now: Director of SICCA Denmark. Part of multinational Sjogren project.

2010 - now: Director of Osteonecrosis Research at Copenhagen University Hospital, Denmark.

2010 - now: Director of Copenhagen ONJ Cohort (288 patients)

2011 – now: Scandinavian Coordinator for Scandinavian ONJ Database (Amgen XGEVA-363-study). 1000 patients enrolled.

2014 – now: European Lead Investigator for a Global Multicenter Case registry ONJ study (Amgen 2010-1102 study).

PUBLICATIONS ON MRONJ (SYMPOSIUM SPEAKERS) IN CHRONOLOGIC ORDER

2018

Aljohani S, Gaudin R, Weiser J, Tröltzsch M, Ehrenfeld M, Kaeppler G, Smeets R, **Otto S**. Osteonecrosis of the jaw in patients treated with denosumab: A multicenter case series. *J Craniomaxillofac Surg*. 2018 May 31. doi: 10.1016/j.jcms.2018.05.046.

Schiødt M, Vadhan-Raj S, Chambers MS, **Nicolatou-Galitis O**, Politis C, Coropciuc R, **Fedele S**, Jandial D, Zhang J, Ma H, Saunders DP. A multicentre case registry on medication-related osteonecrosis of the jaw in patients with advanced cancer. *Support Care Cancer*. 2018 Jun; 26(6):1905-15. doi: 10.1007/s00520-017-4003-2.

Herlofson BB, Kjølle GK, Westgaard KL, Lønndalen A, Bruland Ø. Osteonecrosis of the jaw in a bone metastatic cancer patient after long-term bisphosphonate treatment with severe deterioration following radium-223. *Clin Genitourin Cancer*. 2018 May 16. doi: 10.1016/j.clgc.2018.05.003

Abel H, Nielsen C, **Schiødt M**. Medication related osteonecrosis of the jaws associated with targeted therapy as monotherapy and in combination with antiresorptives. A report of 7 cases from the Copenhagen Cohort. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018 Feb;125(2):157-63. doi: 10.1016/j.oooo.2017.10.010

2017

Fung P, Bedogni G, **Bedogni A**, Petrie A, Porter S, Campisi G, Bagan J, Fusco V, Saia G, Acham S, Musto P, Petrucci MT, Diz P, Colella G, Mignogna MD, Pentenero M, Arduino P, Lodi G, Maiorana C, Manfredi M, Hallberg P, Wadelius M, Takaoka K, Leung YY, Bonacina R, **Schiødt M**, Lakatos P, Taylor T, De Riu G, Favini G, Rogers SN, Pirmohamed M, Nicoletti P; GENVABO Consortium, **Fedele S**. Time to onset of bisphosphonate-related osteonecrosis of the jaws: a multicentre retrospective cohort study. *Oral Dis*. 2017 May;23(4):477-83. doi: 10.1111/odi.12632.

Ristow O, **Otto S**, Geiß C, Kehl V, Berger M, Troeltzsch M, Hohlweg-Majert B, Pautke C. Comparison of auto-fluorescence and tetracycline fluorescence for guided bone surgery of medication-related osteonecrosis of the jaw: a randomized controlled feasibility study. *Int J Oral Maxillofac Surg*. 2017 Feb;46(2):157-66. doi: 10.1016/j.ijom.2016.10.008.

2016

Troeltzsch M, Cagna D, Stähler P, Probst FA, Kaeppler G, Troeltzsch M, Ehrenfeld M, **Otto S**. Clinical features of peri-implant medication-related osteonecrosis of the jaw: is there an association with



peri-implantitis. *J Craniomaxillofac Surg*. 2016 Dec;44(12):1945-51. doi: 10.1016/j.jcms.2016.09.018

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Di Fede O, **Bedogni A**, Giancola F, Saia G, Bettini G, Toia F, D'Alessandro N, Firenze A, Matranga D, **Fedele S**, Campisi G. BRONJ in patients with rheumatoid arthritis: a multicenter case series. *Oral Dis*. 2016 Sep;22(6):543-8. doi: 10.1111/odi.12490.

Acquavella J, Ehrenstein V, **Schiødt M**, Heide-Jørgensen U, Kjellman A, Hansen S, Wexell CL, **Herlofson BB**, Noerholt SE, Ma H, Öhrling K, Hernandez RK, Sørensen HT. Design and methods for a Scandinavian pharmacovigilance study of osteonecrosis of the jaw and serious infections among cancer patients treated with anti-resorptive agents for the prevention of skeletal related events. *Clin Epidemiol* 2016;8:267-72. doi: 10.2147/CLEP.S107270.

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Fusco V, **Bedogni A**, Addeo A, Campisi G. Definition and estimation of osteonecrosis of jaw (ONJ), and optimal duration of antiresorptive treatment in bone metastatic cancer patients: supplementary data from the denosumab extension study? *Support Care Cancer*. 2017 Feb;25(2):345-9. doi: 10.1007/s00520-016-3147-9

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Khullar SM, Katebi N, **Herlofson BB**, Tvedt D, Olsen BR. Evidence to support the hypothesis of tuberculosis as a cause of extreme osteonecrosis and osteomyelitis of the mandible in a West African population. *Int J Oral Maxillofac Surg* 2016; 45(12):1600-6. doi:10.1016/j.ijom.2016.06.013

Krüger TB, **Herlofson BB**, Landin MA, Reseland JE. Alendronate alters osteoblast activities. *Acta Odontol Scand* 2016 Oct;74(7):550-7. doi: 10.1080/00016357.2016.1217041

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2015

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10.1016/j.ijom.2015.01.026.

Vescovi P, Giovannacci I, **Otto S**, Manfredi M, Merigo E, Fornaini C, Nammour S, Meleti M. Medication-Related Osteonecrosis of the Jaws: An Auto-Fluorescence Guided Surgical Approach Performed with Er:YAG laser. *Photomed Laser Surg.* 2015 Aug;33(8):437-42. doi: 10.1089/pho.2015.3927

Otto S, Tröltzsch M, Jambrovic V, Panya S, Probst F, Ristow O, Ehrenfeld M, Pautke C. Tooth extraction in patients receiving oral or intravenous bisphosphonate administrations – a trigger for BRONJ development? *J Craniomaxillofac Surg.* 2015 Jul; 43(6):847-54. doi: 10.1016/j.jcms.2015.03.039

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Ottesen C, Gotfredsen K, Wetterslev J, **Morten Schiødt**. Drug-holiday of antiresorptive medication in relation to tooth extractions in cancer patients. Importance for development of osteonecrosis? Danish Dental Jr. 2015;119:940-5.

Nicolatou-Galitis O, Razis E, Galiti D, Galitis E, Labropoulos S, Tsimpidakis A, Sgouros J, Karampeazis A, Migliorati C. Periodontal disease preceding osteonecrosis of the jaw (ONJ) in cancer patients receiving antiresorptives alone or combined with targeted therapies: report of 5 cases and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol 2015 Dec;120(6):699-706. doi: 10.1016/j.oooo.2015.08.007.

Fung PL, Nicoletti P, Shen Y, Porter S, **Fedele S**. Pharmacogenetics of Bisphosphonate-associated Osteonecrosis of the Jaw. Oral Maxillofac Surg Clin North Am. 2015 Nov;27(4):537-46. doi: 10.1016/j.coms.2015.06.005.

Fedele S, Bedogni G, Scoletta M, Favia G, Colella G, Agrillo A, Bettini G, Di Fede O, Oteri G, Fusco V, Gabriele M, Ottolenghi L, Valsecchi S, Porter S, Fung PP, Saia G, Campisi G, **Bedogni A**. Up to a quarter of patients with osteonecrosis of the jaw associated with antiresorptive agents remain undiagnosed. Br J Oral Maxillofac Surg. 2015 Jan;53(1):13-7. doi: 10.1016/j.bjoms.2014.09.001.

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