AO Foundation

Berton Rahn Research Award

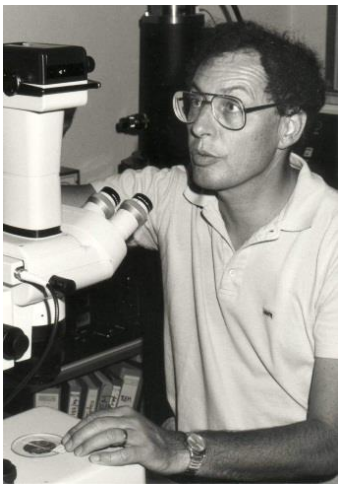
Prof Dr med Dr med dent Berton Albert Anton Rahn
(1939-2008)

Background

The 'Berton Rahn Research Award' was established in recognition of Berton Rahn's immense contribution to the AO Foundation. The prize previously honored the best completed AO Start-up grant project of that year (based upon final reports and the publications resulting from all completed studies). Since 2017, the award is now open to any AO funded research. From August 2018, there is no longer an age limit for the award. The award consists of a keynote presentation at ARI's eCM conference (along with free registration, accommodation and travel to Davos) and a certificate.

Berton A Rahn

Here we inform you briefly about the Berton Rahn and his dedication to the Laboratory for Experimental Surgery Davos (LECD) and its continuation as AO Research Institute Davos (ARI), the AOCMF community and to the AO Foundation itself.



On March 26, 2008, Prof Dr med Dr med dent Berton Rahn passed away after a difficult illness. We as the AO Foundation family lost a friend, mentor and collaborator who dedicated himself to research for the Foundation in Davos. Berton was a highly respected scientist whose morphological-based bone histology is world-renowned and frequently used in AO courses, though often unperceived by those who use and benefit from it. At the 2009 Trustees Meeting in Chicago, the former AO Research Fund Prize Award, which annually honors the best external start-up research fund project, was renamed the Berton Rahn Research Fund Prize Award in honor of his many contributions to the AO Foundation.

Berton grew up in Schaffhausen, Switzerland and first studied dentistry in Zürich until 1964 and medicine in Berlin until 1968. In 1968 he then joined the Laboratory for Experimental Surgery (now ARI) in Davos under the Directorship of Prof Stephan Perren. Berton stayed with AO for over 37 years. Berton received his doctorate in dentistry in 1970, followed by one in medicine in 1973. He qualified as an assistant professor and in 1985 became an associate professor at the University of Freiburg in Germany. In addition to his lecturing responsibilities at the university, he gave lectures on bone healing mainly based on his own research work, at the AO Courses in Davos and worldwide. He also contributed chapters on bone biology and fracture healing to several respected books. His animal studies in sheep on healing of mandibular fractures (1970–1972) were extremely important because they showed that the healing pattern in craniofacial bones (membraneous bones) is the same as in postcranial bones.

Berton was extremely interested in the microscopic pathology (histology) of bone healing and developed polychrome sequence labeling for newly formed bone (1969), used today worldwide in bone research. This technique also led to a decrease in the number of animals needed for research models. Berton also had strong interest in all forms of microscopy and interactions of cells within tissues and with cells and tissues to implants. Berton made important contributions to the development of craniomaxillofacial surgery as well as to the important field of dental implantology. The correction of deformed and damaged maxillofacial structures using Illizarov's distraction method took some fundamental steps forward thanks to the clinical application of Berton Rahn's research. Berton was an active member of many societies and helped place AO Research on the world map. He was one of the original council members of the European Society for Biomaterials (ESB), helped organize their meeting in Davos in 1984 and 1993 and was chosen as an

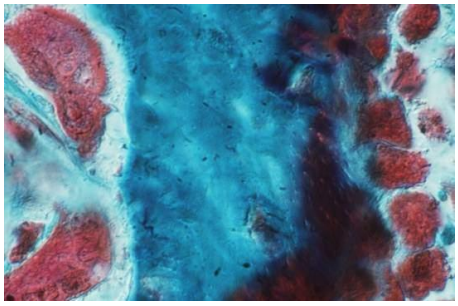
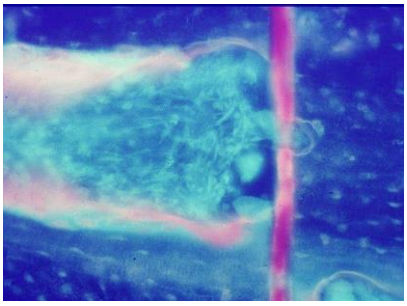
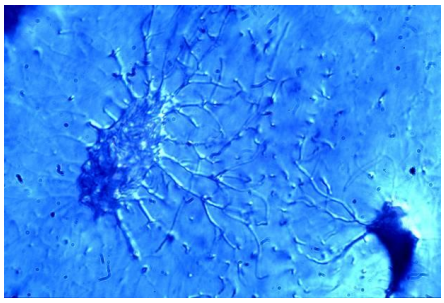
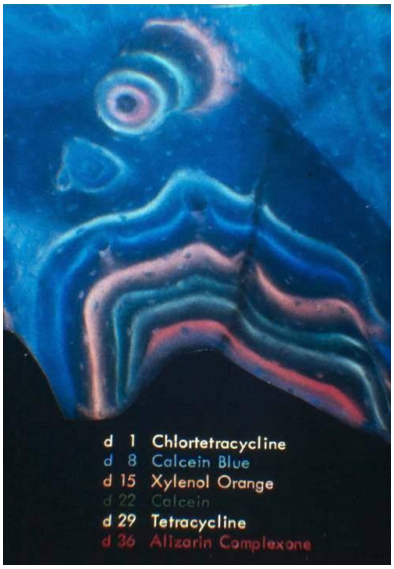
honorary member in 2003. Berton was an author of more than 150 papers and has had several dozens of students pass through his hands, many of them earning their doctoral degree with his help. He always listened to his student's problems and liked to help them to solve these issues through their own reasoning. His research was characterized by its creativity, and above all by the support he offered to young researchers (including Geoff Richards in the early 90's).

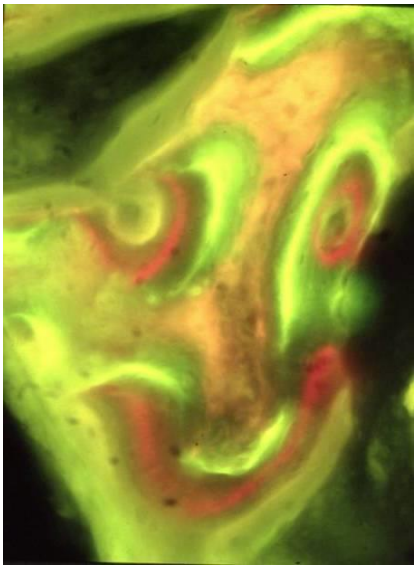
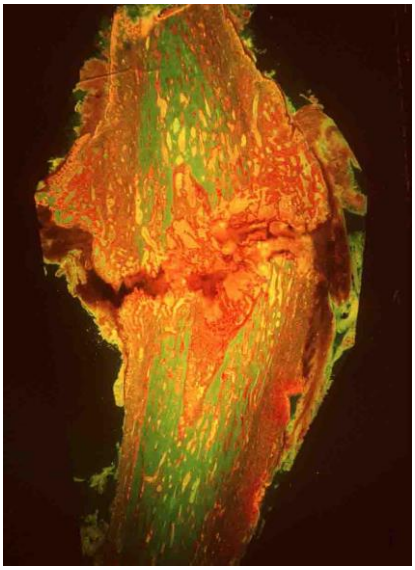
Berton was vice-director of the ARI (from 1975 onwards) and was intimately involved in the design and building of the AO Center on Clavadelerstrasse in Davos which opened in 1992, 20 years ago from this trustee meeting.

Berton was a reserved, sensitive man, but one who in the right moment could surprise with his unique dry sense of humor. His profound humanity made being in his company a great pleasure. In his short duration of retirement, he served as a Scientific Advisor to ARI until the symptoms of his illness manifested themselves in his bones, the very part of the body that he had spent a lifetime studying.

Berton's influence throughout the formative years of the AO Research Institute Davos, and the AO Foundation as a whole, is remembered with deep gratitude.

Prof R Geoff Richards, Director AO Research & Development
Prof Dr med Stephan M Perren, Honorary & Founding Member AO Foundation, past Director LECD & ARI
Prof Dr med Joachim Prein, Honorary Trustee, AO Foundation

Berton Rahn Research Award Winner 2019:

Biographical sketch

Willem-Jan Metsemakers

Willem-Jan Metsemakers is currently a Trauma Surgeon in the department of Trauma Surgery of the University Hospitals Leuven (UZ Leuven), Belgium. He studied medicine at the Catholic University Leuven (KU Leuven) where he graduated in 2007 (MD). In 2014 he was accepted into the medical research fellowship program at the AO Research Institute in Davos, Switzerland. During his fellowship, he worked within the Musculoskeletal Infection Group on experimental models of implant-related infection. This preclinical research was part of his PhD, which was complimented by clinical studies that focused on complications (i.e. infection and compromised fracture healing) after intramedullary nailing. He received his PhD in Biomedical Sciences from the KU Leuven in 2015. He became an assistant professor at the faculty of Medicine (KU Leuven) in 2016.

His current clinical focus is musculoskeletal infection, compromised fracture healing and limb reconstruction in orthopaedic trauma surgery. Within the UZ Leuven he is head of the care program for musculoskeletal infections and member of the antibiotic therapy policy group. As an assistant professor at the KU Leuven he currently supervises PhD students that perform research in the field of infection.

On an international level, Willem-Jan Metsemakers is involved in multiple research projects on the topic of musculoskeletal infection. Most of this research is performed in close collaboration with the AO Foundation and the KU Leuven. He already received local, national and internal scientific research grants (e.g. European Union: JPI-EC-AMR-JTC2018, Antibiofilm therapy through the local administration of bacteriophages / KU Leuven, C3: In vivo validation of the resistance-proof activity of 2-aminoimidazole based anti-biofilm coatings for medical implants), in the field of infection. Within the AO Foundation, he is a member of the Clinical Priority Program on bone infection (AOTrauma) and of the Anti-Infection Task Force (AITF) which is a cross-specialty group within the AOTK System. He is one of the initiators and chairs of the Fracture-Related Infection (FRI) Consensus Group. Over the past years this expert group developed a consensus on diagnostic criteria and treatment principles for FRI. In reflecting the greater complexity of this question, and to engage with other professional organizations, this group has grown over the years to include other external partners. Joining the AO Research Institute, AOTrauma and the AOTK AITF, was the European Bone and Joint Infection Society (EBJIS), the Orthopaedic Trauma Association (OTA), and the Pro-Implant Foundation, as well as a broadened panel of experts with extensive clinical experience in FRI.

Willem-Jan Metsemakers authored over 40 peer-reviewed publications and has given over 200 presentations, invited lectures and webinars. He is an established AO faculty member and chairperson, chairing multiple AOTrauma seminars on bone infection. Furthermore, he is an official reviewer for international scientific journals (e.g. Clinical Infectious Diseases, Journal of Bone and Joint Surgery, Journal of Orthopaedic Trauma, Archives of Orthopaedic and Trauma Surgery).

Fracture-Related Infection: translating scientific evidence to solve current clinical bedside problems

Fracture-related infection (FRI) is currently one of the most challenging complications in trauma surgery. It may result in permanent functional loss or even amputation of the affected limb in patients who may otherwise be expected to achieve complete, uneventful healing. Over the past decades, the problem of implant-related bone infections has garnered increasing attention both in the clinical as well as in the preclinical arenas; however, this has primarily focused on prosthetic joint infection (PJI), rather than on FRI. Although FRI shares many similarities with PJI, there are numerous critical differences (e.g. the presence of

a fracture and soft tissue damage). Over the recent decade preclinical and clinical research has belatedly focused more and more on FRI.

The development of a rabbit fracture model at the AO Research Institute, initiated a series of preclinical studies purely focusing on clinically relevant questions with respect to FRI. One of the first studies focused on the influence of implant material and surface topographies on infection rates. These experimental studies concluded that there is no significant difference between stainless steel and titanium. More recent studies, using this same model, focused on the influence of systemic and local antibiotic therapy on the prevention of infection. It became clear that local antibiotic therapy is an important factor in the prevention of FRI, in highly contaminated wounds. The newly development hydrogel in the AO Research Institute could, in this respect, be an interesting local delivery vehicle, as it is biodegradable and has an optimal release profile. Although this translational evidence is clearly relevant, implementation in daily clinical practice remains difficult due to the lack of standardized guidelines regarding diagnosis and treatment of FRI. The quality of preclinical and clinical research related to fracture-related complications suffers from this lack of consensus guidelines. This recently led to the decision to develop the FRI consensus group, a broadened panel of experts with extensive preclinical and clinical experience in the field of FRI.

One of the first issues addressed was the development of standardized terminology and diagnostic criteria for FRI. Therefore, a first consensus meeting was convened in Davos, Switzerland, in December 2016. During this meeting a consensus was achieved on the fundamental features of FRI, and a proposal for defining the presence of FRI was reached. The establishment of this definition offers the opportunity to standardize preclinical research, improves the reporting of clinical studies and finally of course also aids in the decision-making during daily clinical practice. In the following 12 months, the expert group shifted attention to the next phase, validating the diagnostic criteria and develop treatment principles for FRI. As part of this ongoing effort, the AO Foundation hosted a second consensus meeting on the diagnosis and treatment of FRI in Zürich, Switzerland, in February 2018. In reflecting the greater complexity of this question, and to engage with other professional organizations, the group grew, and the meeting was attended by 35 experts and key opinion leaders in the field of FRI. Recommendations were developed on diagnosis and treatment of FRI. These guiding principles will be made available through scientific publications and an AO Bone Infection App. The whole project is a milestone achievement, where multiple international organizations have come together for the first time to try and improve the care for patients with FRI.

Relevant references

FRI Consensus Group

1. Govaert GAM, Kuehl R, Atkins BL, Trampuz A, Morgenstern M, Obremskey WT, Verhofstad MHJ, McNally MA, Metsemakers WJ (FRI Consensus Group). Diagnosing Fracture-Related Infection: Current concepts and recommendations. J Orthop Trauma. 2019 (submitted).
2. Metsemakers WJ, Morgenstern M, Senneville E, Borens O, Govaert GAM, Onsea J, Depypere Richards RG, Trampuz A, Verhofstad MHJ, Kates SL, Raschke M, McNally MA, William T. Obremskey WT (FRI Consensus group). General treatment principles for fracture-related infection: recommendations for international care bundles. J Orthop Trauma. 2019 (submitted).
3. Metsemakers WJ, Fragomen AT, Moriarty TF, Morgenstern M, Egol KA, Zalavras C, Obremskey WT, Raschke M, McNally MA (FRI consensus group). Local antimicrobial strategies and dead space management in Fracture-Related Infection. J Orthop Trauma. 2019 (submitted).
4. Marais LC, Hungerer S, Eckardt H, Obremskey WT, Ramsden A, McNally MA, Morgenstern M, Metsemakers WJ (FRI Consensus Group). Key aspects of Soft Tissue Management in Fracture-Related Infection. J Orthop Trauma. 2019 (submitted).
5. Depypere M, Kuehl R, Metsemakers WJ, Senneville E, McNally MA, Obremskey WT, Zimmerli W, Atkins BL, Trampuz A (FRI Consensus group). Recommendations for antimicrobial therapy in fracture-related infection: a consensus from an international expert group. J Orthop Trauma. 2019 (submitted).
6. Bezstarosti H, Van Lieshout EMM, Voskamp LW, Kortram K, Obremskey W, McNally MA, Metsemakers WJ, Verhofstad MHJ. Insights into treatment and outcome of fracture-related infection: a systematic literature review. Arch Orthop Trauma Surg. 2019 Jan;139(1):61-72.
7. van den Kieboom J, Bosch P, Plate JDJ, IJpma FFA, Kuehl R, McNally MA, Metsemakers WJ, Govaert GAM. Diagnostic accuracy of serum inflammatory markers in late fracture-related infection. Bone Joint J. 2018 Dec;100-B(12):1542-1550.
8. Onsea J, Depypere M, Govaert G, Kuehl R, Vandendriessche T, Morgenstern M, McNally M, Trampuz A, Metsemakers WJ. Accuracy of Tissue and Sonication Fluid Sampling for the Diagnosis of Fracture-Related Infection: A Systematic Review and Critical Appraisal. J Bone Jt Infect. 2018 Aug 10;3(4):173-181.
9. Morgenstern M, Athanasou NA, Ferguson JY, Metsemakers WJ, Atkins BL, McNally MA. The value of quantitative histology in the diagnosis of fracture-related infection. Bone Joint J. 2018 Jul;100-B(7):966-972.
10. Morgenstern M, Kühl R, Eckardt H, Acklin Y, Stanic B, Garcia M, Baumhoer D, Metsemakers WJ. Diagnostic challenges and future perspectives in fracture-related infection. Injury. 2018 Jun;49 Suppl 1:S83-S90.
11. Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, Athanasou NA, Ochsner PE, Kuehl R, Raschke M, Borens O, Xie Z, Velkes S, Hungerer S, Kates SL, Zalavras C, Giannoudis PV, Richards RG, Verhofstad MHJ. Fracture-related infection: A consensus on definition from an international expert group. Injury. 2018 Mar;49(3):505-510.
12. Metsemakers WJ, Kortram K, Morgenstern M, Moriarty TF, Meex I, Kuehl R, Nijs S, Richards RG, Raschke M, Borens O, Kates SL, Zalavras C, Giannoudis PV, Verhofstad MHJ. Definition of infection after fracture fixation: A systematic review of randomized controlled trials to evaluate current practice. Injury. 2018 Mar;49(3):497-504.
13. Morgenstern M, Moriarty TF, Kuehl R, Richards RG, McNally MA, Verhofstad MHJ, Borens O, Zalavras C, Raschke M, Kates SL, Metsemakers WJ. International survey among orthopaedic trauma surgeons: Lack of a definition of fracture-related infection. Injury. 2018 Mar;49(3):491-496.
14. Metsemakers WJ, Kuehl R, Moriarty TF, Richards RG, Verhofstad MHJ, Borens O, Kates S, Morgenstern M. Injury. 2018 Mar;49(3):511-522.
15. Metsemakers WJ, Moriarty TF, Morgenstern M, Kuehl R, Borens O, Kates S, Richards RG, Verhofstad M. Letter to the Editor: New Definition for Periprosthetic Joint Infection: From the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res. 2016 Dec;474(12):2726-2727.

Translational Research

16. Vallejo A, von Deimling C, Morgenstern M, D'Este M, Pützler J, Zeiter S, Arens D, Metsemakers WJ, Eglin D, Richards RG, Moriarty TF. Local application of a gentamicin-loaded hydrogel early after injury is superior to peri-operative systemic prophylaxis in a rabbit open fracture model. J Orthop Trauma. 2019.
17. Vanvelk N, Morgenstern M, Moriarty TF, Richards RG, Nijs S, Metsemakers WJ. Preclinical in vivo models of fracture-related infection: a systematic review and critical appraisal. Eur Cell Mater. 2018 Oct 17;36:184-199.
18. Puetzler J, Metsemakers WJ, Arens D, Zeiter S, Kuehl R, Raschke MJ, Richards RG, Moriarty TF. Antibiotic Prophylaxis With Cefuroxime: Influence of Duration on Infection Rate With Staphylococcus aureus in a Contaminated Open Fracture Model. J Orthop Trauma. 2018 Apr;32(4):190-195
19. Moriarty TF, Kuehl R, Coenye T, Metsemakers WJ, Morgenstern M, Schwarz EM, Riool M, Zaat SAJ, Khana N, Kates SL, Richards RG. Orthopaedic device-related infection: current and future interventions for improved prevention and treatment. EFORT Open Rev. 2017 Mar 13;1(4):89-99.
20. Ter Boo GA, Arens D, Metsemakers WJ, Zeiter S, Richards RG, Grijpma DW, Eglin D, Moriarty TF. Injectable gentamicin-loaded thermo-responsive hyaluronic acid derivative prevents infection in a rabbit model. Acta Biomater. 2016 Oct 1;43:185-194.
21. Metsemakers WJ, Moriarty TF, Nijs S, Pape HC, Richards RG. Influence of implant properties and local delivery systems on the outcome in operative fracture care. Injury. 2016 Mar;47(3):595-604.
22. Metsemakers WJ, Schmid T, Zeiter S, Ernst M, Keller I, Cosmelli N, Arens D, Moriarty TF, Richards RG. Titanium and steel fracture fixation plates with different surface topographies: Influence on infection rate in a rabbit fracture model. Injury. 2016 Mar;47(3):633-9.
23. Metsemakers WJ, Emanuel N, Cohen O, Reichert M, Potapova I, Schmid T, Segal D, Riool M, Kwakman P, de Boer L, de Breij A, Nibbering P, Richards RG, Zaat SAJ, Moriarty TF. A doxycycline–loaded lipid-and-polymer-based drug delivery coating for the prevention of implant-related osteomyelitis due to doxycycline-resistant methicillin-resistant Staphylococcus aureus. J control Release. 2015;209:47-56.

Previous Berton Rahn Research Award Winners

2018

CRP Annulus Fibrosus Rupture (AFR): (ANNUPHEN)

Characterization of intervertebral disc cells and identification on a suitable cell source for efficient tissue regeneration

Daisuke Sakai, Tokai University School of Medicine in Kanagawa, Japan

2017

CRP Acute Cartilage Injury (ACI): (HiCartia)

A novel platform for optimizing material design for cartilage tissue engineering and enabling drug discovery for cartilage restoration

Robert Mauck, University of Pennsylvania (USA)

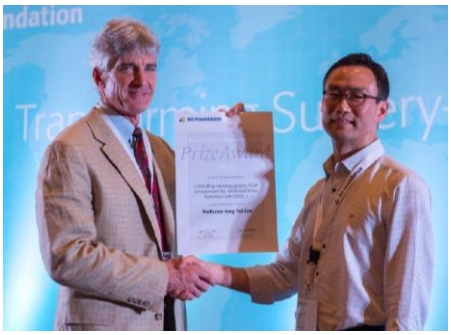
2016

Project S-12-27S:

Targeting endothelial to mesenchymal transition in fibrodysplasia ossificans progressive

Gonzalo Sánchez Duffhues, Leiden University Medical Center (NL)

2015



Project S-10-07L:

Controlling nanotopography-ECM environment for enhanced bone formation with hMSCs

Jung Yul Lim, University of Nebraska-Lincoln (USA)

2014

Project S-10-62Y:

Stem cell mobilization for enhanced bone healing

Clare Yellowley, University of California Davis (USA)

2013

Project S-07-1C:

Can low intensity pulsed ultrasound accelerate osteoporotic fracture healing?

Wing-Hoi Cheung, The Chinese University of Hong Kong (China)

2012

Project S-05-95J:

In-situ crosslinkable osteoinductive poly(lactide) scaffold for bone regeneration

Esmaiel Jabbari, University of South Carolina (USA)

2011

Project F-07-43L:

A pilot study of interleukin-12 local delivery for infection prevention after a traumatic open fracture

Bingyun Li, West Virginia University (USA)

2010

Project 04-J44:

Skeletal effects of estrogen

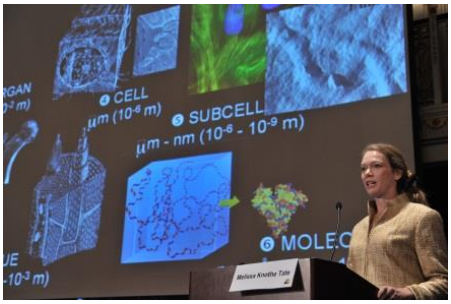
Teppo Järvinen, University of Tampere (Finland)

2009 (2 winners)

Project 04-I58:

Effects of cyclic compression on intervertebral disc cell metabolism

James C Iatridis, University of Vermont (USA)



Project 04-K3:

Unravelling endogenous mechanisms of bone regeneration through quantification of the interplay between bone cells and their environment

Melissa Knothe Tate, Cleveland Clinic Foundation (USA)