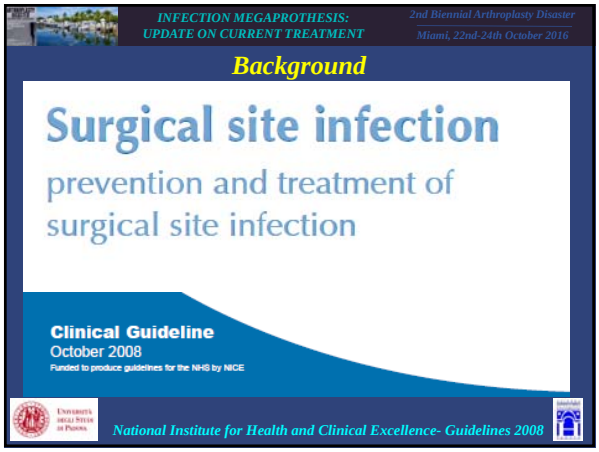

2nd Biennial Arthroplasty Disaster International Conference
Miami | 22nd-24th October, 2016
Infection Megaprothesis:
Update on Current Treatment
P. Ruggieri, G. Trovarelli
Department of Orthopedics and Orthopedic Oncology, University of Padova, Italy


INFECTION MEGAPROTHESIS:
UPDATE ON CURRENT TREATMENT
2nd Biennial Arthroplasty Disaster
Miami, 22nd-24th October 2016
Background
Surgical site infection
prevention and treatment of
surgical site infection
Clinical Guideline
October 2008
Funded to produce guidelines for the NHS by NICE
National Institute for Health and Clinical Excellence- Guidelines 2008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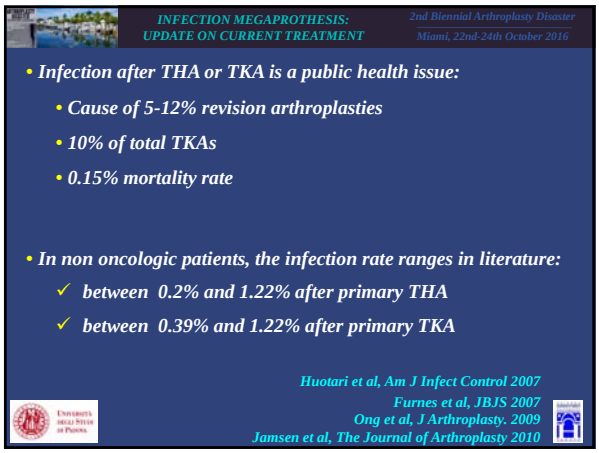
Background
Clinical practice guidelines for antimicrobial prophylaxis in surgery
250 citations
IDSA GUIDELINES
Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America
260 citations
4.6 IF
Bratzler DW et al, ASHP Guidelines 2013
Osmon DR et al, IDSA Guidelines 2013


INFECTION MEGAPROTHESIS:
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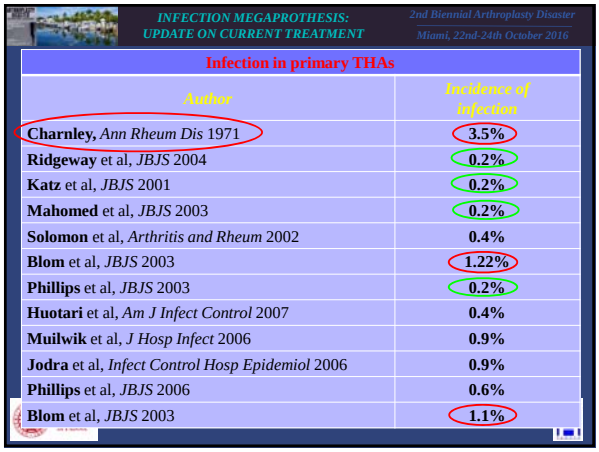
• Infection after THA or TKA is a public health issue:
• Cause of 5-12% revision arthroplasties
• 10% of total TKAs
• 0.15% mortality rate
• In non oncologic patients, the infection rate ranges in literature:
✓ between 0.2% and 1.22% after primary THA
✓ between 0.39% and 1.22% after primary TKA
Huotari et al, Am J Infect Control 2007
Furnes et al, JBJS 2007
Ong et al, J Arthroplasty. 2009
Jamsen et al, The Journal of Arthroplasty 2010


INFECTION MEGAPROTHESIS:
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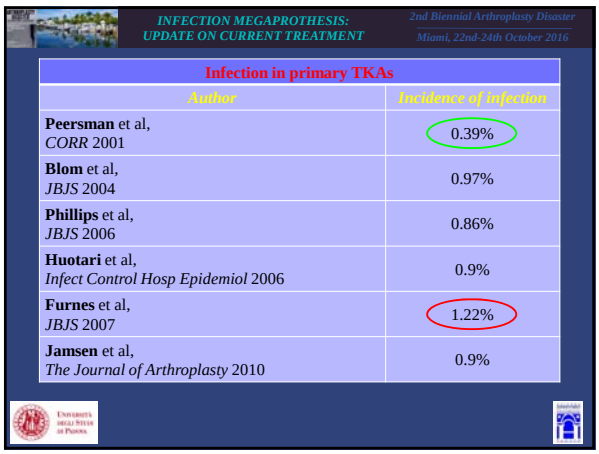
Infection in primary THAs
Author
Incidence of infection
Charnley, Ann Rheum Dis 1971 3.5%
Ridgeway et al, JBJS 2004 0.2%
Katz et al, JBJS 2001 0.2%
Mahomed et al, JBJS 2003 0.2%
Solomon et al, Arthritis and Rheum 2002 0.4%
Blom et al, JBJS 2003 1.22%
Phillips et al, JBJS 2003 0.2%
Huotari et al, Am J Infect Control 2007 0.4%
Muilwik et al, J Hosp Infect 2006 0.9%
Jodra et al, Infect Control Hosp Epidemiol 2006 0.9%
Phillips et al, JBJS 2006 0.6%
Blom et al, JBJS 2003 1.1%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Infection in primary TKAs
Author
Incidence of infection
Peersman et al, CORR 2001 0.39%
Blom et al, JBJS 2004 0.97%
Phillips et al, JBJS 2006 0.86%
Huotari et al, Infect Control Hosp Epidemiol 2006 0.9%
Furnes et al, JBJS 2007 1.22%
Jamsen et al, The Journal of Arthroplasty 2010 0.9%

Infection of tumor prostheses is a major concern because of:

- ✓ *extensive soft-tissue dissection*
- ✓ *prolonged surgical times*
- ✓ *immunosuppression due to chemotherapy*

The infection rate ranges in literature between 3.7% and 19.9%

Mittermayer et al, CORR 2001
Zeegen et al, CORR 2004
Jacofsky et al, CORR 2004
Gosheger et al, CORR 2006
Sharma et al, CORR 2007
Funovics et al, Int Orthop 2010
Schwartz et al, CORR 2010
Henderson et al, JBJS 2011
Healey et al, CORR 2013
Pala et al, CORR 2015

Professor Kotz 1970 - 2011

The First to Develop a Metallic
Modular Endoprosthesis for Musculoskeletal Tumor Surgery

Modular Megaprostheses Kotz I

One of the Leaders in Expandable Prosthesis in Immature Skeleton

Howmedica Segmental Tumor Prosthesis 1987

Eckardt

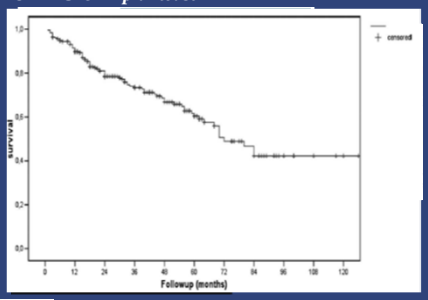
Malawer

Stryker systems

Kotz et al, Orthopade 2010
Pala et al, CORR 2015

Tumor modular prosthetic systems

- MUTARS ® Implantcast



Georg Gosheger

W. Winkelmann

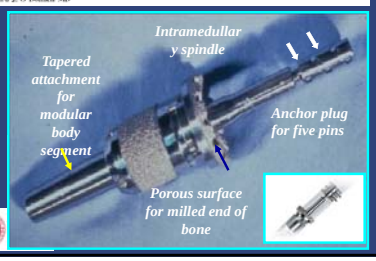
Gosheger G and Winkelmann W, Orthopade 2000
Gosheger G et Al, CORR 2006

Tumor modular prosthetic systems

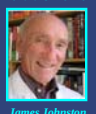
- Compress ® system

Compressive Osseointegration of Tibial Implants in Primary Cancer Reconstruction

Richard J. O'Donnell MD



Richard O'Donnell



James Johnston

John Healey

O'Donnell RJ, CORR 2009

Tumor modular prosthetic systems

- Stanmore ® System

Modular endoprosthetic replacement for tumours of the proximal femur

Proximal femur reconstruction
100 cases (2001-2006)

ASEPTIC LOOSENING IN CEMENTED CUSTOM-MADE PROSTHETIC REPLACEMENTS FOR BONE TUMOURS OF THE LOWER LIMB

P. S. UNWIN, S. R. CANNON, R. J. GRIMER, H. B. S. KEMP, R. S. SNEATH, P. S. WALKER

From the Royal National Orthopaedic Hospital Trust, Stanmore and the Royal Orthopaedic Hospital, Birmingham, England

1001 patients! Low aseptic loosening rate

Chandrasekar CR et al., JBJS Br. 2009
Unwin P et Al., JBJS Br 1996


Stephen Cannon


Robert Grimer


Paul Unwin


Lee Jeys

Tumor modular prosthetic systems

- System – C Link ® system


Rodolfo Capanna

Campanacci et al, ISOLS 2013

Reconstructive options in Limb Salvage

Results

Limb salvage	Pts	Re-Op rate	Major Revision / Conversion rate	Amputation rate
Massive allografts	52	50.0%	23.1%	3.4%
Endoprostheses	172	29.1%	7.0%	4.1%
		p=0.005	p=0.001	p=0.943

Ward . W. EMSOS meeting 2013
22 yrs experience of Guthrie Clinic, Sayre, PA, USA

Infection in the literature

Author	Pts	Sites	Mean FU	Infection
Mittermayer et al. CORR 2001	100	Lower limb	1982 - 1989 127.5 months	9.7%
Zeegen et al. CORR 2004	141	Lower and upper limb	1993 - 2001 1.5 years	14%
Jacofsky et al. CORR 2004	42	Proximal femur	1980 – 2000 5.8 yrs (15 days-20 yrs)	10%
Gosheger et al. CORR 2006	250	Lower and upper limb	1992 - 2003 45 months (3–140 months)	12%
Sharma et al. CORR 2007	135	Lower and upper limb	57 months (1.4 -157 months)	8%
Schwartz et al CORR 2010	186	Distal femur	1980 - 2008 96 months (1-336 months)	3.7%
Henderson et al JBJS 2011	2174	Lower and upper limb	1974 - 2008	8.4%
Healey et al. CORR 2013	82	Knee	1998 - 2008 43 months (6-131 months)	6%
Pala et al. CORR 2015	247	Knee	2003 - 2010 5 years (2-7 years)	9.3%
Mavrogenis et al. Surgical infections 2015	1161	Lower limb	1983 – 2010 9 years (3–20 years)	8.6%

≈10%

SURGICAL INFECTIONS
Volume X, Number X, 2015
© Mary Ann Liebert, Inc.
DOI: 10.1089/sur.2014.085

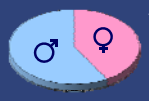
Infected Prostheses after Lower-Extremity Bone Tumor Resection: Clinical Outcomes of 100 Patients

Andreas F. Mavrogenis, Elisa Pala, Andrea Angelini, Teresa Calabro, Carlo Romagnoli, Matteo Romantini, Gabriele Drago, and Pietro Ruggieri

Mavrogenis et al, Surgical infections 2015

Patients and Methods

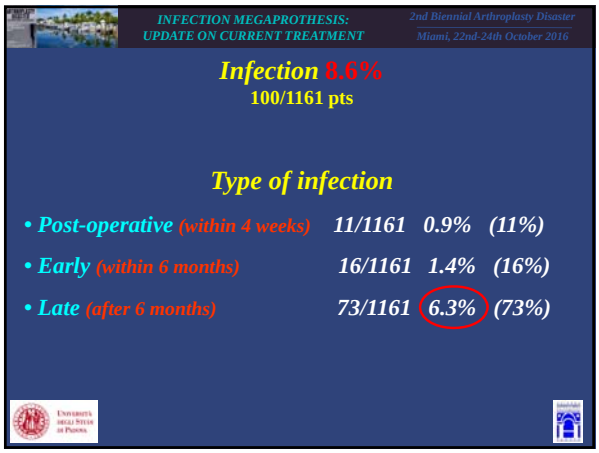
1161 pts (1983 – 2010)



Mean age 31.2 yrs

Site of reconstruction

- Distal femur 743 (64%)
- Proximal tibia 226 (19.5%)
- Proximal femur 154 (13.3%)
- Total femur 29 (2.5%)
- Extrarticular knee resection 9 (0.8%)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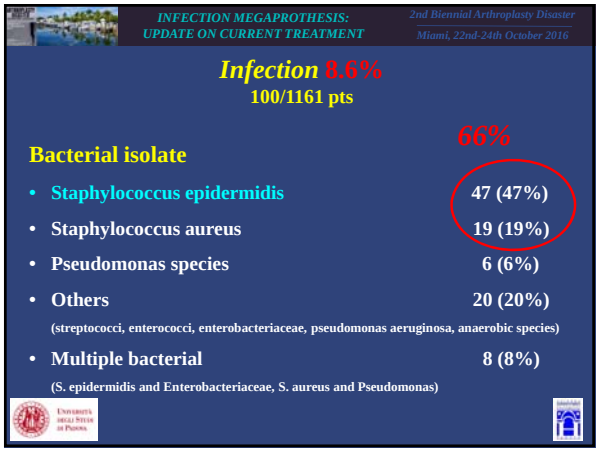
Infection 8.6%
100/1161 pts
Type of infection
• Post-operative (within 4 weeks) 11/1161 0.9% (11%)
• Early (within 6 months) 16/1161 1.4% (16%)
• Late (after 6 months) 73/1161 6.3% (73%)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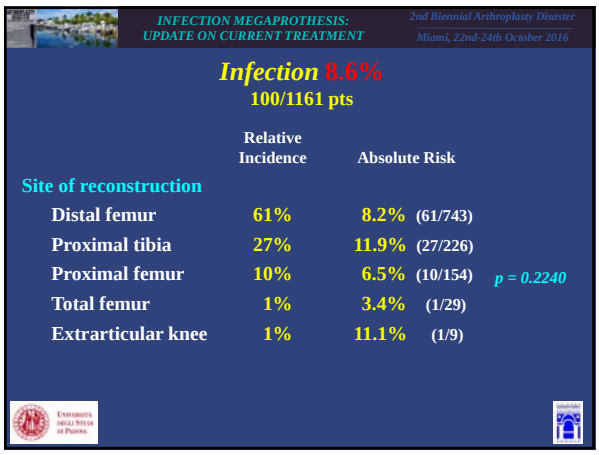
Infection 8.6%
100/1161 pts
66%
Bacterial isolate
• Staphylococcus epidermidis 47 (47%)
• Staphylococcus aureus 19 (19%)
• Pseudomonas species 6 (6%)
• Others 20 (20%)
(streptococci, enterococci, enterobacteriaceae, pseudomonas aeruginosa, anaerobic species)
• Multiple bacterial 8 (8%)
(S. epidermidis and Enterobacteriaceae, S. aureus and Pseudomonas)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Infection 8.6%
100/1161 pts
Relative Incidence
Absolute Risk
Site of reconstruction
Distal femur 61% 8.2% (61/743)
Proximal tibia 27% 11.9% (27/226)
Proximal femur 10% 6.5% (10/154) p = 0.2240
Total femur 1% 3.4% (1/29)
Extrarticular knee 1% 11.1% (1/9)

Infection 8.6%

100/1161 pts

	Relative Incidence	Absolute Risk	
Type of megaprostheses			
KMFTR fixed hinge	18%	11.3% (18/160)	
HMRS fixed hinge	56%	8.6% (56/653)	p = 0.3075
HMRS rotating hinge	6%	8.8% (6/68)	
GMRS rotating hinge	20%	7.1% (20/280)	

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Infection 8.6%

	Relative Incidence	Absolute Risk	
Type of fixation			
Cementless	91%	8.5% (91/1067)	p = 0.0460
Cemented	9%	9.6% (9/94)	
	Relative Incidence	**Absolute Risk**	
Adjuvant treatments			
Radiotherapy and/or chemotherapy	70%	8.8% (70/799)	p = 0.5480
No adjuvant treatments	30%	8.3% (30/362)	

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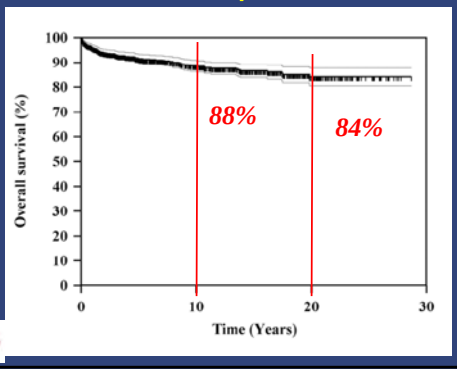
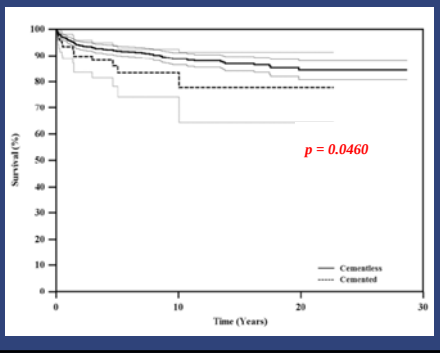
Survival to infection



Survival to infection according to stem fixation



Treatment of infection

Type of treatment

One-stage revision	12/100	12%
Two-stage revision	83/100	83%
Amputation (first treatment)	5/100	5%

Treatment of infection

Outcome of the infection

Complete resolution (overall)	75/100	75%
acute infections	8/11	72.7%
early infections	11/16	68%
late infections	56/73	76.6%
Recurrence of infection	25/100	25%
Amputation for recurrence of infection	16/100	16%
Amputation for infection (overall)	21/100	21%

11 Centers in :

Bologna
Brescia

Catania
Gorizia
Milano
Messina
Roma
Torino

Padova

MUTARS System: The Italian Experience

INFECTION MEGAPROTHESIS: UPDATE ON CURRENT TREATMENT
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MUTARS System: The Italian Experience

1996:	First MUTARS Implant (Prof. Rosa, Cath.Univ, Gemelli H., Rome)
1997:	Rizzoli Inst. (IOR), Bologna
2000:	Brescia
2003:	Sicily (Messina, Taormina)
2005:	G.Pini Inst., Milano
2007:	IFO (Rome), Napoli
2008:	Gorizia, Humanitas (MI)
2009:	Galeazzi Inst. (Milano)
2010:	Torino

925 Implants up to Aug. 2013

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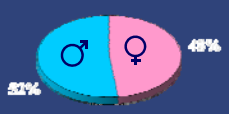
MUTARS System: The Italian Experience

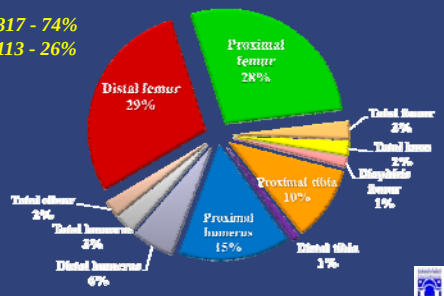
430 cases (2000 – 2013)



Mean age 50.4 yrs (range: 4-85 yrs)
Males 226, females 204

MUTARS System: The Italian Experience

Lower limbs 317 - 74%
Upper limbs 113 - 26%



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MUTARS System: The Italian Experience

Types of prostheses

- *Standard* 244
- *Silver coated* 186
- *Inverse shoulder* 15
- *X-pand* 12

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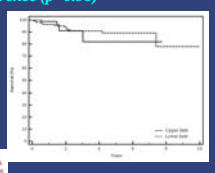
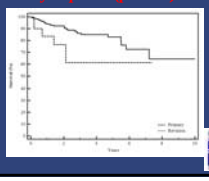
MUTARS System: The Italian Experience

Infection: 23/430 (5.3%)
Mean interval of 1.5 yrs

- *18/317 (5.6%) Lower limb*
- *5/113 (4.4%) Upper limb*
- *No difference (p=0.98)*



- *5/43 (11.6%) Revision*
- *18/368 (4.9%) Primary*
- *Significant better survival for primary implants (p= 0.02)*



MUTARS System: The Italian Experience

Infection: 23/430 (5.3%)

Mean interval of 1.5 yrs

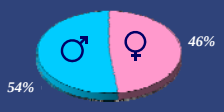
- *14/244 (5.7%) Standard prostheses*
- *9/186 (4.8%) Silver coated*
- *One way Anova, p = 0.08*

- *15 two stage (2 amputations)*
- *1 one stage*
- *6 amputations*
- *1 arthrodesis*

- *8/23 (35%): Amputation*

MUTARS prostheses

157 cases (2000 – 2016) in three Centers



Mean age 50.4 yrs (range: 4-84 yrs)

Males 85, females 72

MUTARS System: IOR-COOBS experience

Types of implant

- *Cemented 52 (46.8%) → 22/38 upper limb*
  30/73 lower limb
- *Press-fit 59 (53.2%) → 16/38 upper limb*
  43/73 lower limb

- *Primary 96 (86.5%)*
- *Revisions 15 (13.5%)*

- *Inverse Sh. 8*
- *X-pand 2*
- *Silver 58*

Failures: 40 cases (25.5%)

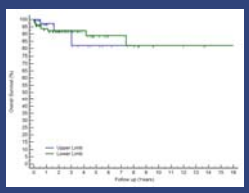
At a mean time of 1.7 years

	N. of cases	Relative incidence	Absolute risk
Mechanical	15	37.5%	9.5%
Non-Mechanical	25	62.5%	15.9%
Type 1 Soft tissue failure	5	12.5%	3.2%
Type 2 Aseptic loosening	7	17.5%	4.5%
Type 3 Structural failure	3	7.5%	1.9%
Type 4 Infection	13	32.5%	8.3%
Type 5 umor progression	12	30%	7.6%

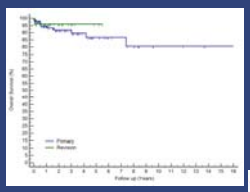
Infection: 13/157 (8.3%)

Mean time of 1.5 yrs

- Lower limb 10/105 (9.5%)
- Upper limb 3/52 (5.7%)
- *No difference (p = 0.991)*



- Revision 3/31 (9.6%)
- Primary 10/126 (9.7%)
- *No difference (p = 0.531)*



Infection: 13/157 (8.3%)

Mean time of 1.5 yrs

Treatment

- 8 two stage (then 1 amputation)
- 1 one stage
- 3 amputation
- 1 arthrodesis

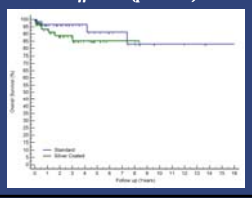
- 4/13 (30%): Amputation

- Cemented 6/74 (8.1%)
- Press fit 7/83 (8.4%)

No difference (p = 0.785)

- Silver coated 8/77 (10.4%)
- Standard 5/80 (6.2%)

No difference (p = 0.247)



MOFFITT CANCER CENTER

ISTITUTO ORTOPEDICO RIZZOLI

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Elisa Pala M.D.

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Philipp Funovics M.D.

MIAMI

Thomas Temple M.D.

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THE JOURNAL OF BONE & JOINT SURGERY

JB&JS

Failure Mode Classification for Tumor Endoprostheses: Retrospective Review of Five Institutions and a Literature Review

By Eric R. Henderson, MD, John S. Groundland, MS, PT, Elisa Pala, MD, Jeremy A. Dennis, BS, Rebecca Wooten, PhD, David Cheong, MD, Reinhard Windhager, MD, Rainer I. Kotz, MD, Mario Mercuri, MD, Philipp T. Funovics, MD, Francis J. Hornicek, MD, PhD, H. Thomas Temple, MD, Pietro Ruggieri, MD, and G. Douglas Letson, MD

Investigation performed at the Sarcoma Program, H. Lee Moffitt Cancer and Research Institute, Tampa, Florida; Orthopaedic Oncology Division, Department of Orthopaedic Surgery, University of Miami, Miami, Florida; Division of Orthopaedic Oncology, Massachusetts General Hospital, Boston, Massachusetts; Istituto Ortopedico Rizzoli, University of Bologna, Bologna, Italy; and Department of Orthopaedic Surgery, Medical University of Vienna, Vienna, Austria

INFECTION MEGAPROTHESIS: UPDATE ON CURRENT TREATMENT
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Classification of Segmental Endoprosthesis Failure

Mechanical	Type 1	Soft Tissue Failure	Instability, tendon rupture, wound dehiscence
	Type 2	Aseptic Loosening	Clinical and radiographic evidence of loosening
	Type 3	Structural Failure	Periprosthetic or prosthetic fracture
Non-Mechanical	Type 4	Infection	Infected endoprosthesis not amenable to retention
	Type 5	Tumor Progression	Recurrence or progression of tumor with endoprosthesis contamination

Henderson et al, JBJS Am 2011

Metanalysis of Orthopaedic Literature

	Oncology Segmental Procedures	Soft Tissue Failure	Aseptic Loosening	Structural Failure	Infection	Recurrent Disease
Proximal Humerus	252	16	16	2	5	39
Total Humerus	9	1	0	2	0	2
Distal Humerus	35	0	2	3	0	12
Proximal Femur	568	16	26	5	32	32
Total Femur	76	0	4	3	14	14
Distal Femur	3011	4	336	172	165	165
Proximal Tibia	717	0	64	52	138	138
DFR and PTR	169	0	19	12	4	4
Total	5133	37(1%)	467 (9%)	251 (5%)	358 (7%)	243 (5%)

Henderson et al, JBJS Am 2011

INFECTION MEGAPROTHESIS: UPDATE ON CURRENT TREATMENT
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Prostheses failures in multicentric studies

Location	Total Procedures	Soft-tissue Failure	Aseptic Loosening	Structural Failure	Infection	Recurrent Disease	Total Failures
Proximal humerus	348	4.0%	2.6%	1.1%	6.3%	2.9%	17%
Total humerus	16	0	0	0	19%	0	19%
Distal humerus	36	0	0	5.6%	5.6%	5.6%	19%
Proximal femur	403	5.2%	2.7%	0.7%	3.0%	4.0%	16%
Total femur	78	9.0%	2.6%	1.3%	12%	2.6%	27%
Distal femur	951	1.3%	6.8%	6.3%	8.3%	4.7%	27%
Extra-artic knee res	44	6.8%	2.3%	6.8%	23%	4.6%	43%
Proximal tibia	298	2.3%	4.7%	6.4%	15%	5.4%	34%
All locations	2174	2.9%	4.7%	4.2%	8.4%	4.3%	24.5%

Henderson et al, JBJS Am 2011

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2nd Biennial Arthroplasty Disaster
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Review Article

CME ARTICLE

Infected Tumor Prostheses

ANDREAS F. MAVROGENIS, MD; PANAYIOTIS J. PAPAGELOPOULOS, MD, DSC; LUIS COLL-MESA, MD; ELISA PALA, MD; GIOVANNI GUERRA, MD; PIETRO RUGGIERI, MD, PHD

Mavrogenis et al, Orthopedics 2011

Treatment of infection

- *Often challenging, with a high number of reoperations required*
  - ✓ *Early diagnosis*
  - ✓ *Appropriate treatment strategy*
  - ✓ *Accurate identification of the responsible pathogens*
  - ✓ *Appropriate antibiotic regimen*

Mavrogenis et al, Orthopedics 2011

Evaluation	Details
Clinical signs	Persistent joint pain, fever, erythema, calor, effusion, sinus
Blood	White blood cell count, C-reactive protein, erythrocyte sedimentation rate
Radiographs, CT scans	Bone loss, loosening (late)
Ultrasonography	Joint effusion, synovial hypertrophy
Radionuclide bone scanning	Leuko[illegible]maging ?
Synovial fluid aspiration	Microbiological examination, *Chemical and physical examination*
Biopsy	Periprosthetic tissue, synovium; histological and microbiological examination
Prosthesis sonication	Microbiological examination
Nucleic amplification techniques	Detection of bacterial 16S ribosomal DNA

Moran et al, J Antimicrob Chemother. 2010
Mavrogenis et al, Orthopedics 2011

Prosthetic sonication

Bogut et al, Pol J Microbiol. 2014
Scorzolini et al, New Microbiol. 2014
Shen et al, J Clin Microbiol. 2015

Treatment of infection

Conservative management:
(debridement without removal prosthetic components)

- Early infections
- Short duration of symptoms
- Well-fixed and functional implant
- Highly susceptible pathogens

➢ **Avoided in:**

- Late infections → poor results (successful in 6%)
- Persisting infection → loosening

Marculescu et al, Clin Infect Dis. 2006

1-stage revision (successful in 42%)

- Early or low-grade infection
- Antibiotic-sensitive pathogens
- Poor general condition of patient
- May caused long delay of chemotherapy
- Within 3-4 weeks from onset of infection

Lee Sh, Oh JH, Lee KH, Kim HS.
Infection after prosthetic reconstruction in limb salvage surgery.
Int Orthop. 2002; 26(3):179-184

Hardes J, Gebert C, Schwappach A et al.
Characteristic and outcome of infection associated with tumor endoprostheses.
Arch Orthop Trauma Surg. 2006; 126(5):289-296

Funovics PT, Hipfl C, Hofstaetter JG, Puchner S, Kotz RI, Dominkus M.
Management of septic complication following modular endoprosthetic reconstruction of the proximal femur.
Int Orthop. 2011; 35(10):1437-1444

Holzer G, Windhager R, Kotz R.
One-stage revisione surgery for infected megaprostheses.
J Bone Joint Surg Am. 1998; 79(1):31-35

2-stage revision (successful in 72% to 91%)

- Persistent and higher grade infections
- Antibiotic-resistant pathogens
- Failed 1-stage procedures

Grimer RJ, Belthur M, Chandrasekar C, Carter SR, Tillman RM.
Two-stage revision for infected endoprostheses used in tumor surgery.
Clin Orthop Relat Res. 2002; (395):193-203

Flint MN, Griffin Am, Bell RS, Wunder JS, Ferguson PC.
Two-stage revision of infected uncemented lower extremity tumor endoprostheses.
J Arthroplasty. 2007; 22(6)859-865

Turcotte R.
Endoprosthetic replacements for bone tumors: review of the most recent literature.
Curr Opin Orthop. 2007; 18(6):572-578

Stockley I, Mockford B, Hoad-Reddick A, Norman P.
The use of two-stage exchange arthroplasty with depot antibiotics in the absence of long-term antibiotic therapy in infected total hip replacement.
J Bone Joint Surg Br. 2008; 90(2):145-148

Amputation (successful in 98% to 100%)

- Risk of amputation between 23.5% and 87%

Jeys LM, Grimer RJ, Carter SR, Tillman RM. Risk of amputation following limb salvage surgery with endoprosthetic replacement, in a consecutive series of 1261 patients. Int Orthop. 2003; 27(3):160-163

Jeys LM, Grimer RJ, Carter SR, Tillman RM. Periprosthetic infection in patients treated for an orthopaedic oncological condition. J Bone Joint Surg Am. 2005; 87(4):842-849

Shehadeh A, Noveau J, Malawer M, Henshaw R. Late complications and survival of endoprosthetic reconstruction after resection of bone tumors. Clin Orthop Relat Res. 2010; 468(11):2885-2895

M, 57 yo, osteoblastic osteosarcoma of the distal femur

Wide resection and megaprosthetic reconstruction with a cemented fixed hinge knee prosthesis plus pre- and postoperative chemotherapy

Removal of the prosthesis and implant of a vancomycin and tobramycin cement spacer for Staphylococcus epidermidis infection after 4 months from surgery

Arthrodesis with a megaprosthesis 6 months later


INFECTION MEGAPROTHESIS:
UPDATE ON CURRENT TREATMENT
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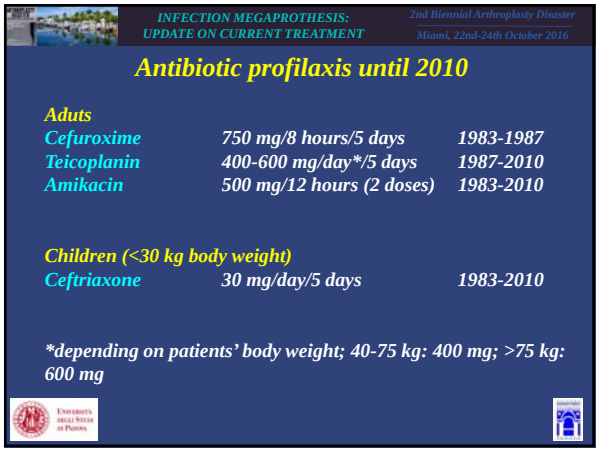
Miami, 22nd-24th October 2016
What we can do
to reduce the risk of infection?
Change Antibiotic profilaxis?
New materials?
Silver coated prostheses?
Betadine binding?
Other?


INFECTION MEGAPROTHESIS:
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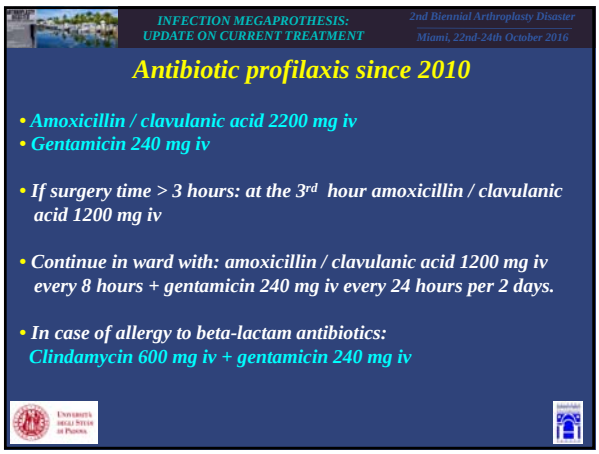
Antibiotic profilaxis until 2010
Aduts
Cefuroxime 750 mg/8 hours/5 days 1983-1987
Teicoplanin 400-600 mg/day*/5 days 1987-2010
Amikacin 500 mg/12 hours (2 doses) 1983-2010
Children (<30 kg body weight)
Ceftriaxone 30 mg/day/5 days 1983-2010
*depending on patients' body weight; 40-75 kg: 400 mg; >75 kg: 600 mg


INFECTION MEGAPROTHESIS:
UPDATE ON CURRENT TREATMENT
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Antibiotic profilaxis since 2010
• Amoxicillin / clavulanic acid 2200 mg iv
• Gentamicin 240 mg iv
• If surgery time > 3 hours: at the 3rd hour amoxicillin / clavulanic acid 1200 mg iv
• Continue in ward with: amoxicillin / clavulanic acid 1200 mg iv every 8 hours + gentamicin 240 mg iv every 24 hours per 2 days.
• In case of allergy to beta-lactam antibiotics:
Clindamycin 600 mg iv + gentamicin 240 mg iv

Antibiotic resistance: 80,000 'might die' in future outbreak

Cabinet Office

National Risk Register of Civil Emergencies

2015 edition

National Risk register of Civil Emergencies, UK, 2015

Perioperative antibiotics prophylaxis

BMJ open

Prophylactic antibiotic regimens in tumour surgery (PARITY): protocol for a multicentre randomised controlled study

Michelle Ghert,[1] Benjamin Deheshi,[1] Ginger Holt,[2] R Lor Randall,[3] Peter Ferguson,[4] Jay Wunder,[4] Robert Turcotte,[5] Joel Werier,[6] Paul Clarkson,[7] Timothy Damron,[8] Joseph Benevenia,[9] Megan Anderson,[10] Mark Gebhardt,[10] Marc Isler,[11] Sophie Mottard,[11] John Healey,[12] Nathan Evaniew,[1] Antonella Racano,[1] Sheila Sprague,[1] Marilyn Swinton,[1] Dianne Bryant,[1] Lehana Thabane,[1] Gordon Guyatt,[1] Mohit Bhandari,[1] The PARITY Investigators

Ghert M et Al, BMJ 2012

How to prevent infections?

- ✓ *Among metals, silver offers good antimicrobial action and low toxicity*
- ✓ *Bacteria are quite susceptible to silver with bactericidal activity*
- ✓ *Silver ions are released from the surface coating and reach antimicrobially effective silver concentrations in the surrounding tissue*
- ✓ *The effect of silver ions is continuous and long lasting*
- ✓ *The ability of many bacteria to produce a biofilm is reduced*

Donlan et al, Clin Microbiol Rev. 2002
Ceri et al, J Clin Microbiol. 1999
Trampuz et al, Rev Med Microbiol. 2003
Isiklar et al, CORR 1996

Silver-coated implants

Reduction of Periprosthetic Infection With Silver-Coated Megaprostheses in Patients With Bone Sarcoma

Research Article

The Influence of Elementary Silver Versus Titanium on Osteoblasts Behaviour In Vitro Using Human Osteosarcoma Cell Lines

Lack of toxicological side-effects in silver-coated megaprostheses in humans

Silver-coated megaendoprostheses in a rabbit model—an analysis of the infection rate and toxicological side effects

Georg Gosheger

There is need for multicentric studies to confirm the role of recent discoveries

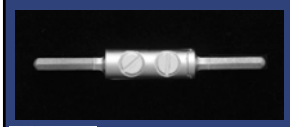
Gosheger et al, Biomaterials 2004
Hardes et al, Biomaterials 2007
Hardes et al, Sarcoma 2007
Hardes et al, J Surg Oncol 2010

Silver-coated megaendoprostheses in a rabbit model—an analysis of the infection rate and toxicological side effects

Georg Gosheger[a,*], Jendrik Hardes[a], Helmut Ahrens[a], Arne Streitburger[a], Horst Buerger[b], Michael Erren[c], Andreas Gunsel[d], Fritz H. Kemper[d], Winfried Winkelmann[a], Christof von Eiff[a]

In silver group (vs. titanium group):

- *Lower infection rates: 7% versus 47%* $p = 0.05$
- *Lower signs of inflammation*
- *Elevated silver concentration in blood and in organs without pathologic changes*



Gosheger et al, Biomaterials 2004

Lack of toxicological side-effects in silver-coated megaprostheses in humans

Jendrik Hardes[a,*,1], Helmut Ahrens[a,1], Carsten Gebert[a], Arne Streitbuerger[a], Horst Buerger[b], Michael Erren[c], Andreas Gunsel[d], Christian Wedemeyer[e], Guido Saxler[e], Winfried Winkelmann[a], Georg Gosheger[a]

- *Silver-coated megaprosthesis allowed a release of silver without showing any local or systemic side-effects.*

- *Galvanic deposition of pure silver releases only low amounts of active silver ions (Ag+) in the surrounding environment depending on the electrochemical setting.*

Hardes et al, Biomaterials 2007

Reduction of Periprosthetic Infection With Silver-Coated Megaprostheses in Patients With Bone Sarcoma

JENDRIK HARDES, MD,[1]* CHRISTOF VON EIFF, MD,[2] ARNE STREITBUERGER, MD,[1] MAURICE BALKE, MD,[1] TYMOTEUS BUDNY, MD,[1] MARCEL P. HENRICHS, MD,[1] GREGOR HAUSCHILD, MD,[1] AND HELMUT AHRENS, MD[1]
[1]Department of Orthopedics and Tumor Orthopedics, Münster University Hospital, Münster, Germany
[2]Institute of Medical Microbiology, Münster University Hospital, Münster, Germany

- *Reduction in infection rate: 5.9% (silver group) vs. 17.6% (titanium group).*
- *Reduction in infection rate in the medium term.*
- *Less aggressive treatment of infection was possible.*

p=0.062
not significant

Hardes et al, J Surg Oncol 2010

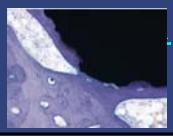
Silver-coated implants

Bone Joint J. 2015 Feb;97-B(2):252-7. doi: 10.1302/0301-620X.97B2.34554.

Retrospective evaluation of the incidence of early periprosthetic infection with silver-treated endoprostheses in high-risk patients: case-control study.

Wafa H[1], Grimer RJ[2], Reddy K[3], Jeys L[2], Abudu A[2], Carter SR[2], Tillman RM[2].

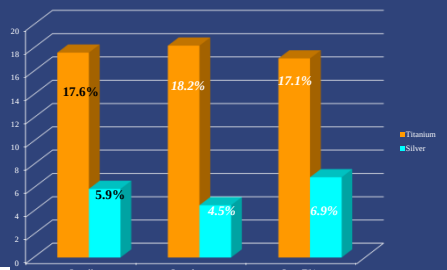
85 "Silver" cases (2006-2011) vs 85 conventional cases (2001-2011)
- lower rate of early infection $p = 0.033$
- particularly useful in two-stage revisions for infection
- Debridement + antibiotic treatment appeared to be more successful



Hauschild et al, Biomed Res Int 2015
Wafa et al, Bone Joint J 2015
Hardes et al, JSO 2010
Hardes et al, Biomaterials 2007
Gosheger G et al, Biomaterials 2004

MUTARS System: the Münster Experience

Infection rate (%)



Time of infection:
81 % in between 24 months postoperatively

Courtesy of J. Hardes, G. Gosheger

Conventional
= X €

Silver Coated (+ 15%)
= X + 1.000 €

1 Deep Inf. Prosth.
= > 48 Silver Coated

Ippolito et al, ISOLS 2013

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SAVINGS:

- **The higher cost of 48 Silver Coated equals the costs of One Single Deep Infection.**
- **If we implant 25 Silver Coated Prostheses and this avoids even one single Deep Infection, the Health System saves about 24.000 €**

Ippolito et al, ISOLS 2013

INFECTION MEGAPROTHESIS: UPDATE ON CURRENT TREATMENT
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Conclusions

- *Megaprosthetic reconstruction after major resection in the lower limb has a high risk of infection*
- *Most frequent bacteria are stafilococcus epidermidis and stafilococcus aureus*
- *Most infections occur as late infections*
- *Risk of infection is unrelated with type of prosthesis*
- *Risk of infection is unrelated with site of reconstruction*
- *Risk of infection is possibly related with multiple surgical procedures*

→ *need for study on infection only after primary procedure*

Conclusions

- *Functional results of treatment of infection are satisfactory*
- *One stage treatment has selected indications, mainly in post-operative infection*
- *Two stage treatment is successful in most cases and recommended in all late infections*
- *Careful checks of lab tests, coltures, intraoperative checks are recommended before re-implantation*
- *Amputations are still required in persistent refractary infections*

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Silver coating seems to work

Multicentric studies needed to confirm data

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Implantcast International Intergroup

Arthroplasty Disaster Conference: infections and complex reconstructions Orlando, 21-22 November 2014


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