



L'Elettrochemioterapia: un nuovo trattamento per le metastasi ossee

Laura Campanacci

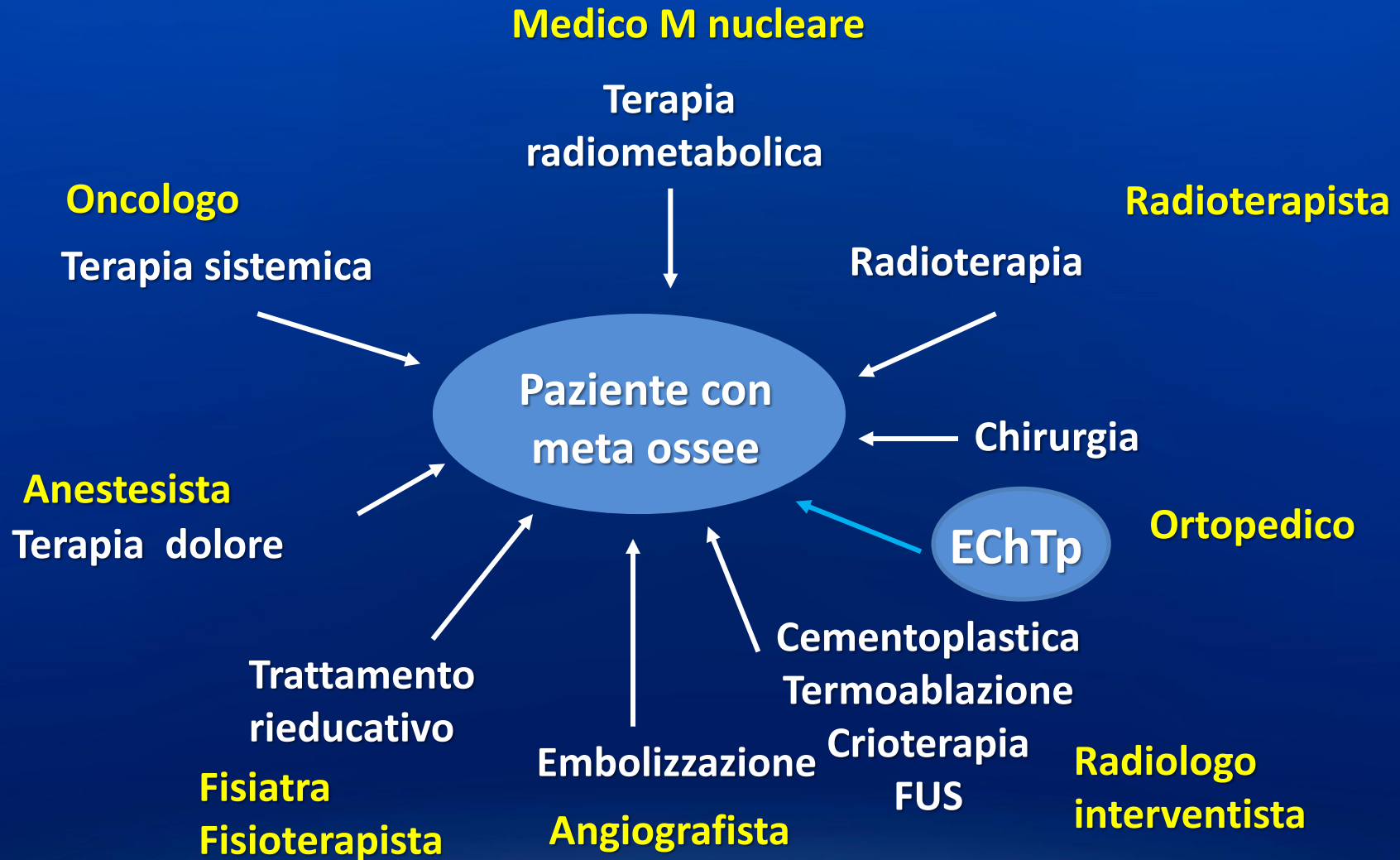
IRCCS Istituto Ortopedico Rizzoli
SC 3 Clinica Ortopedica a prevalente indirizzo Oncologico



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Istituto Ortopedico Rizzoli di Bologna
Istituto di Ricovero e Cura a Carattere Scientifico

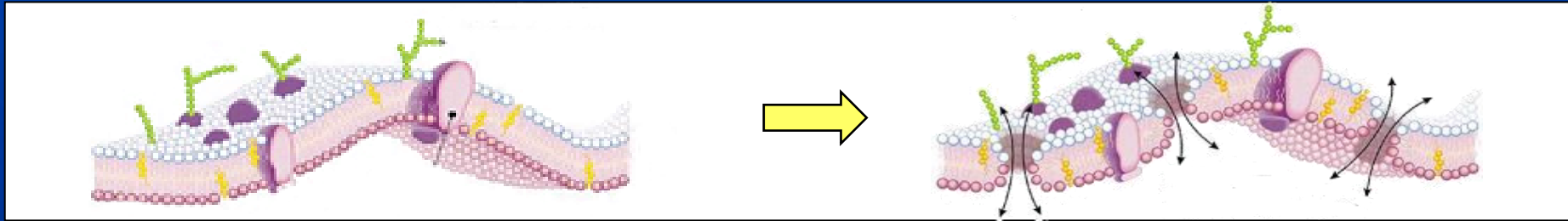


Metastasi Ossea: trattamento multidisciplinare



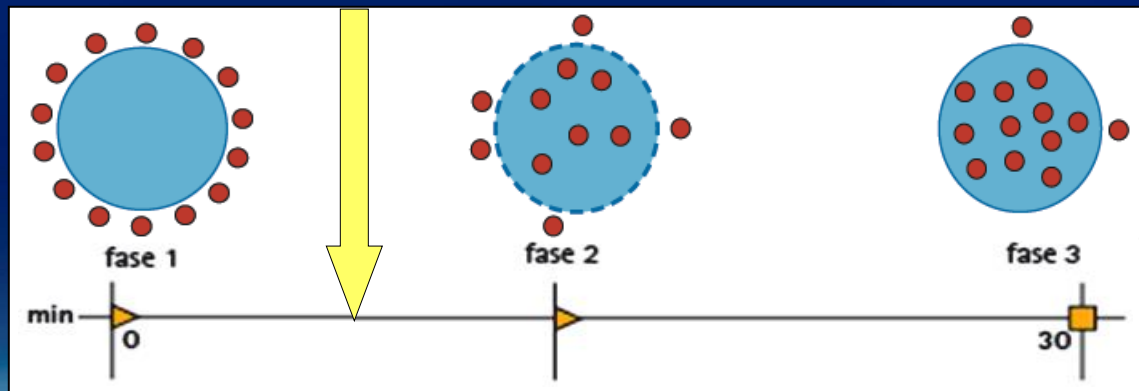
Elettroporazione

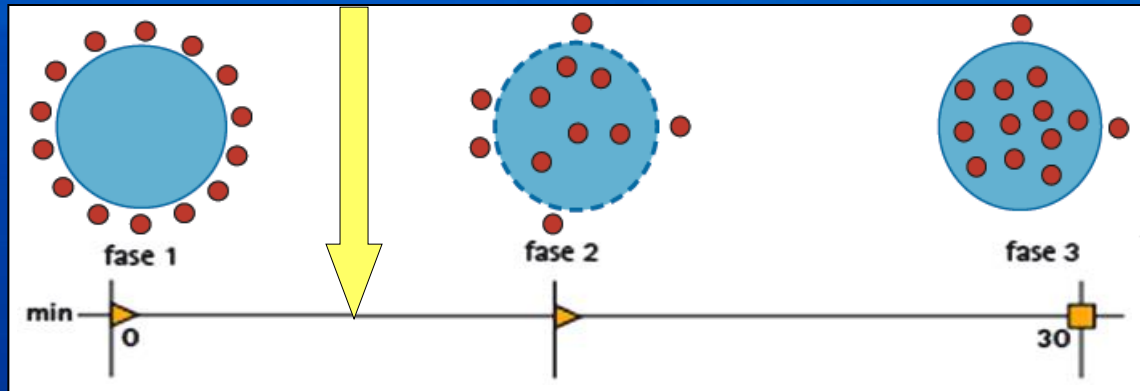
impulsi elettrici intensi e brevi: > permeabilità delle membrane cellulari.



Elettrochemioterapia

L'aumento della permeabilità consente a farmaci per nulla o poco permeanti, di penetrare nel citoplasma ed aumentare la propria intrinseca efficacia intratumorale.





Bleomicina

clinical use of electrochemotherapy.²⁻⁵ Exposure of cells to electric pulses increases cytotoxicity of bleomycin (~8000 fold) and cisplatin (~80 fold).^{2,3}

Azione citotossica: Danno diretto al DNA

Dipende da capacità di entrare nella cellula

Elettroporazione “forza” l’entrata del farmaco nella cellula:

Attività citotossica indipendente da istotipo

EJC SUPPLEMENTS 4 (2006) 3-13

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

ELSEVIER

Electrochemotherapy – An easy, highly effective and safe treatment of cutaneous and subcutaneous metastases: Results of ESOPE (European Standard Operating Procedures of Electrochemotherapy) study

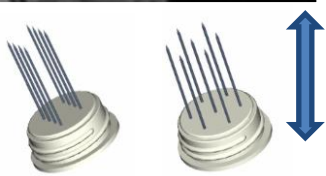
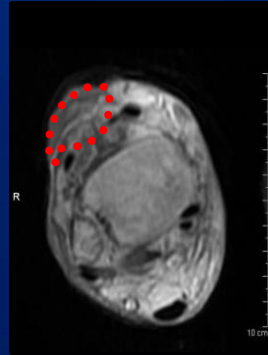
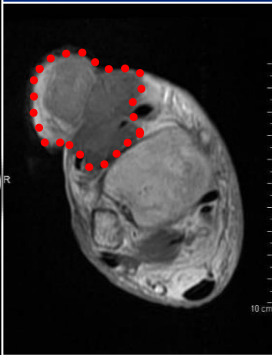
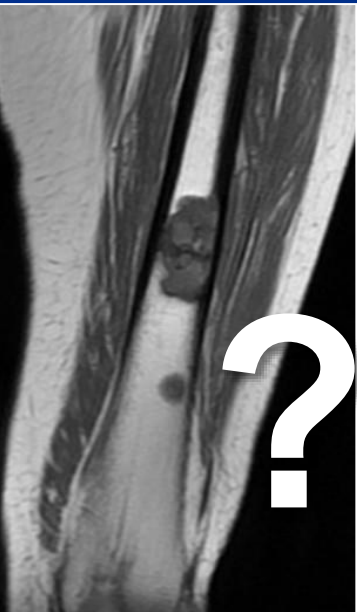
Michel Marty^a, Gregor Sersa^{b,h}, Jean Rémi Garbay^a, Julie Gehl^c, Christopher G. Collins^d, Marko Snoj^b, Valérie Billard^a, Poul F. Geertsen^c, John O. Larkin^d, Damijan Miklavcic^e, Ivan Pavlovic^e, Snezna M. Paulin-Kosir^b, Maja Cemazar^b, Nassim Morsli^a, Declan M. Soden^d, Zvonimir Rudolf^b, Caroline Robert^a, Gerald C. O’Sullivan^d, Lluís M. Mir^{a,f,g,*}

^aInstitut Gustave-Roussy, 39 Rue Camille Desmoulins, F-94805 Villejuif Cedex, France
^bInstitute of Oncology Ljubljana, Zaloška 2, SI-1000 Ljubljana, Slovenia
^cDepartment of Oncology, 54B1, University of Copenhagen at Herlev Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark
^dCork Cancer Research Centre, Mercy Hospital, Greenville Place, Cork, Ireland
^eUniversity of Ljubljana, Faculty of Electrical Engineering, Tržaška 25, SI-1000 Ljubljana, Slovenia
^fCNRS UMR 8121, 39 Rue Camille Desmoulins, F-94805 Villejuif Cedex, France
^gUniv Paris-Sud, UMR 8121, France

ECT: Trattamento Locale

- Non esclude altri trattamenti locali
- Non ritarda trattamento sistemico
 - 1 somministrazione in bolo di Bleomicina (clearance 50% in 3 ore)

ECT per metastasi superficiali (sarcoma/carcinoma/melanoma)

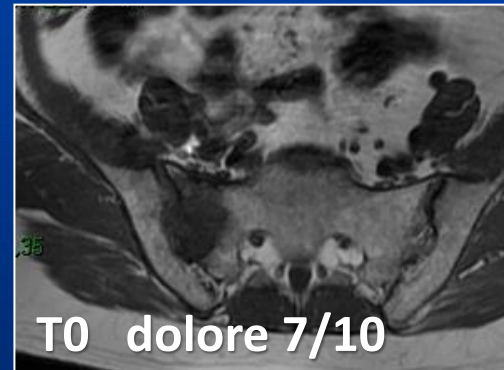
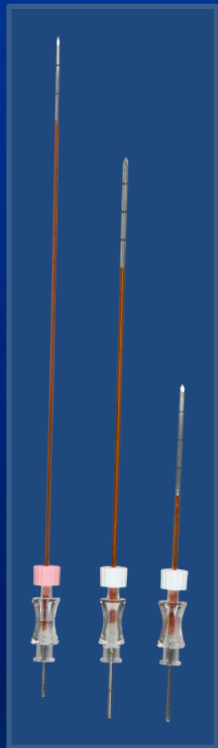


3 cm

ECT Tumori OSSO (> metastasi)

Sviluppo
Tecnologia:

61 aa, metastasi ossee da Leiomiiosarcoma



EP non danneggia le cellule e la matrice dell'osso



■ RESEARCH

Ablation of bone cells by electroporation
J Bone Joint Surg Br. 2010 Nov;92(11):1614-20

M. Fini,
M. Tschon,
M. Ronchetti,
F. Cavani,
G. Bianchi,
M. Mercuri,
M. Alberghini,
R. Cadossi

30 giorni dopo ElettroPORAZIONE: intensa attività osteogenetica nell'osso trabecolare e sulla sua superficie

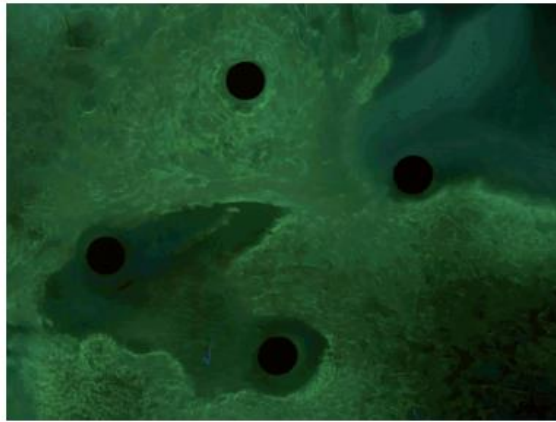


Fig. 6a

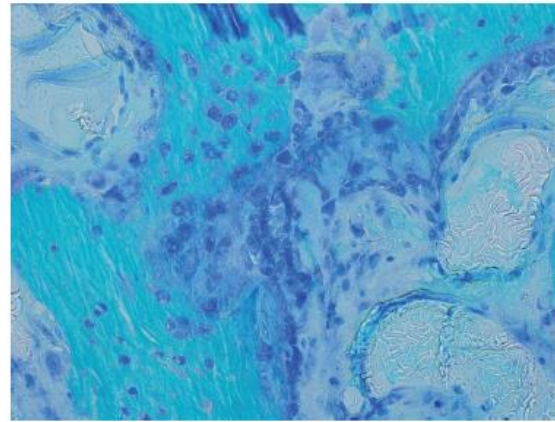


Fig. 6b

Histology of bone tissue of animals killed 30 days after electroporation treatment. Figure 6a – new bone formation evidenced by tetracycline labelling (unstained sections, 1.25x magnification). Figure 6b – intense osteogenic activity is present within trabecular bone and on its surface (toluidine blue and fast green staining, 20x magnification).

Efficacia ECT per trattamento delle Metastasi Ossee

Risposta Radiologica

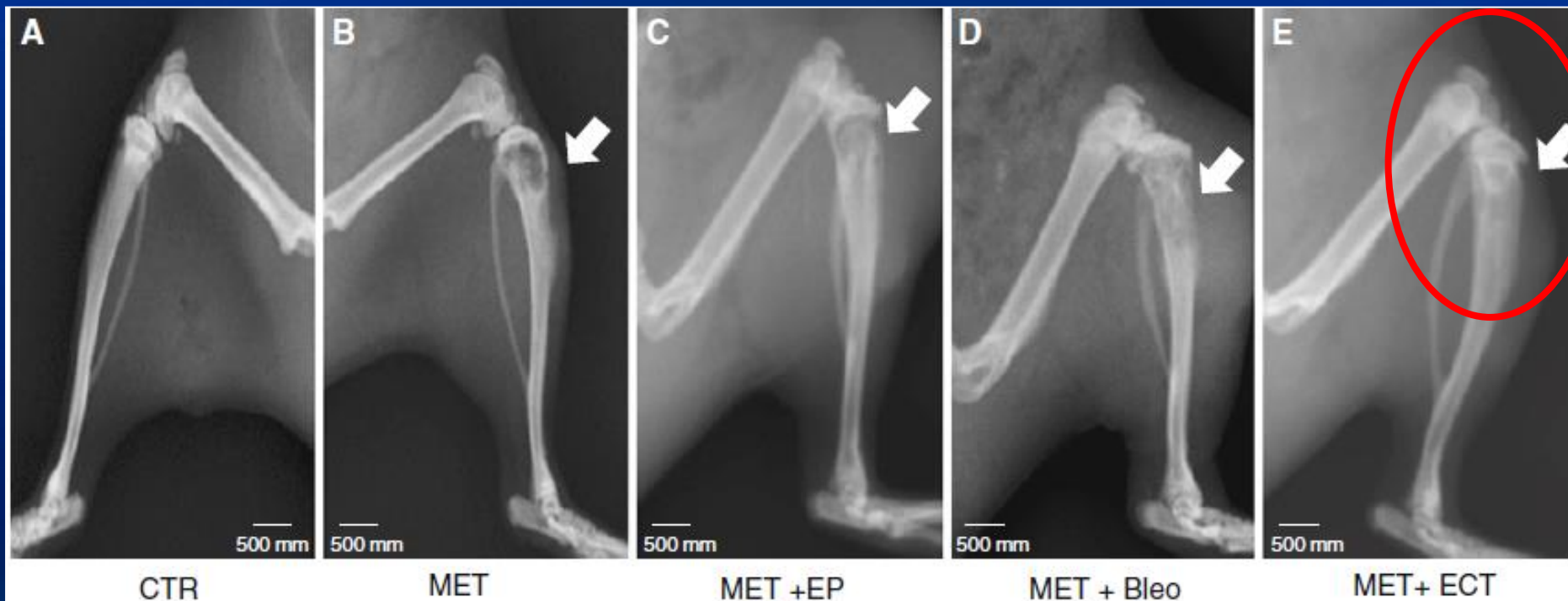
2013

Clin Exp Metastasis (2013) 30:1033–1045
DOI 10.1007/s10585-013-9601-x

RESEARCH PAPER

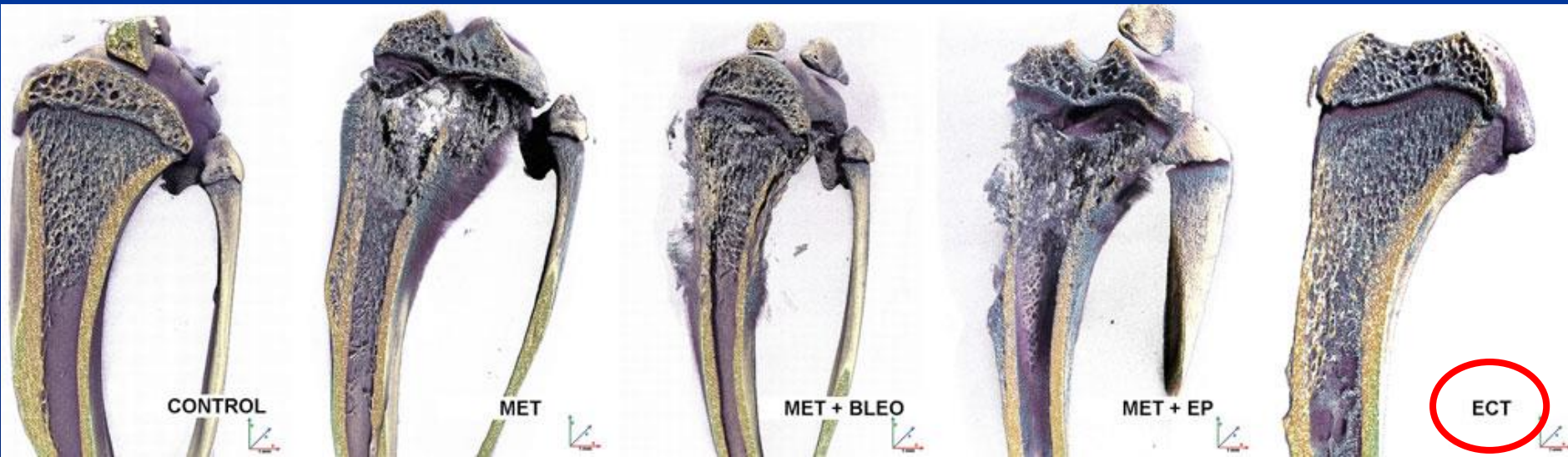
Electrochemotherapy is effective in the treatment of rat bone metastases

Milena Fini • Francesca Salamanna •
Annapaola Parrilli • Lucia Martini •
Matteo Cadossi • Melania Maglio • Veronica Borsari



Efficacia ECT per trattamento delle Metastasi Ossee

Risposta Radiologica

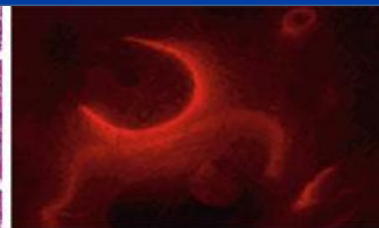
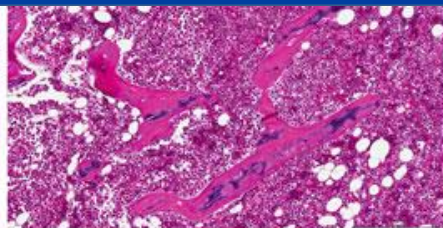
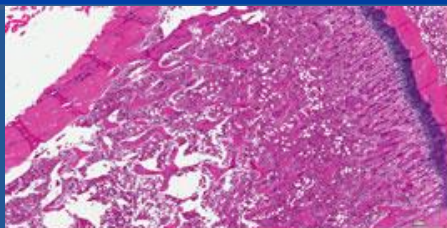


Micro TAC dopo 21 giorni

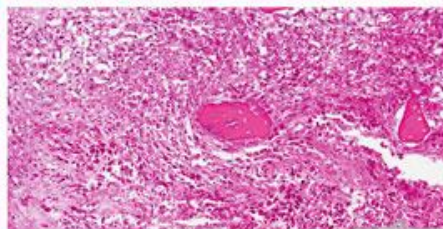
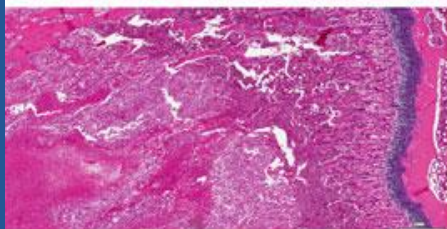
Efficacia ECT per trattamento delle Metastasi Ossee

Attività Osteoblasti dopo 20 giorni

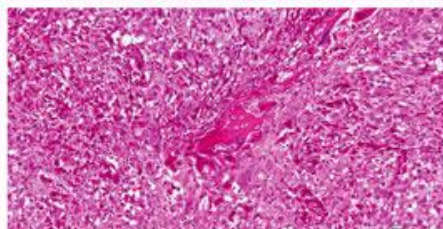
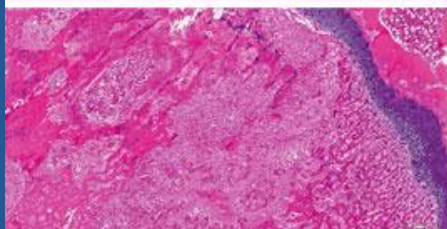
CTR



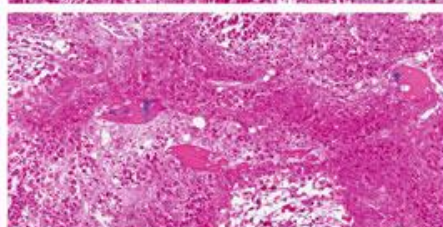
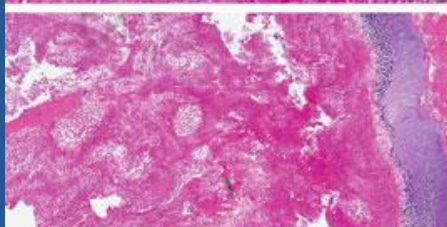
MET



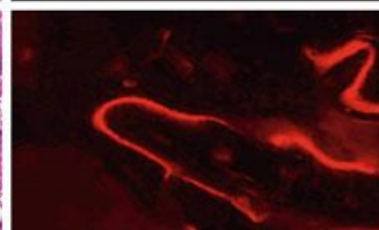
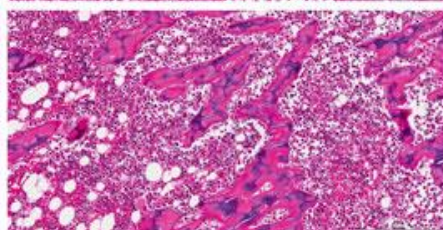
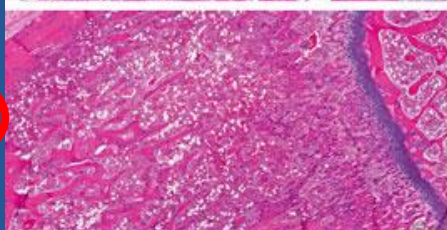
MET+EP



MET+BLEO



MET+ECT





ECT NON danneggia l'osso,
Che rimane vitale a distanza dal trattamento



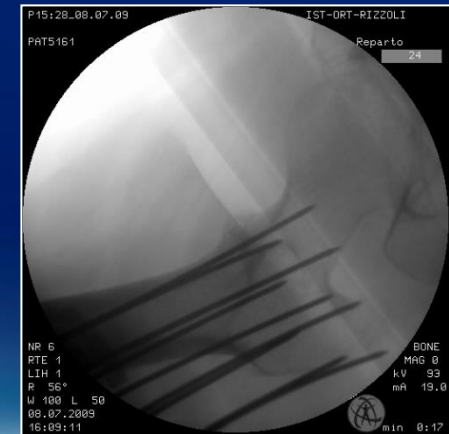
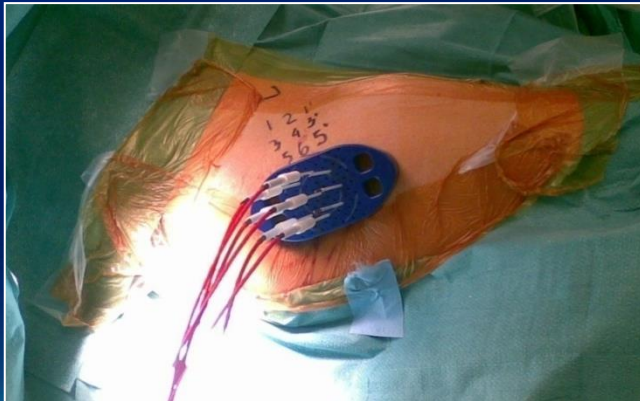
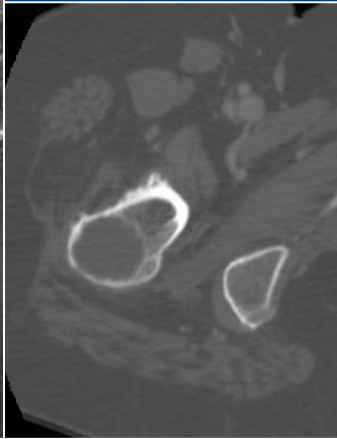
18 mesi dopo ECT



5 anni dopo Radioterapia

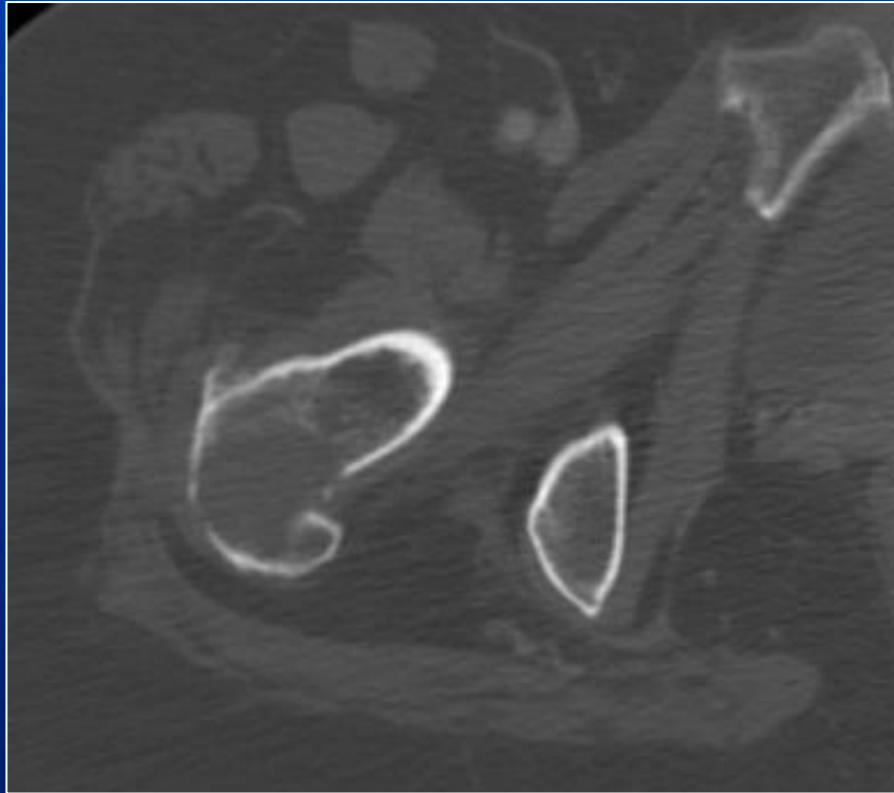
59 anni, Meta Ossee e cerebrali da Ca Renale

Guida Amplioscopica

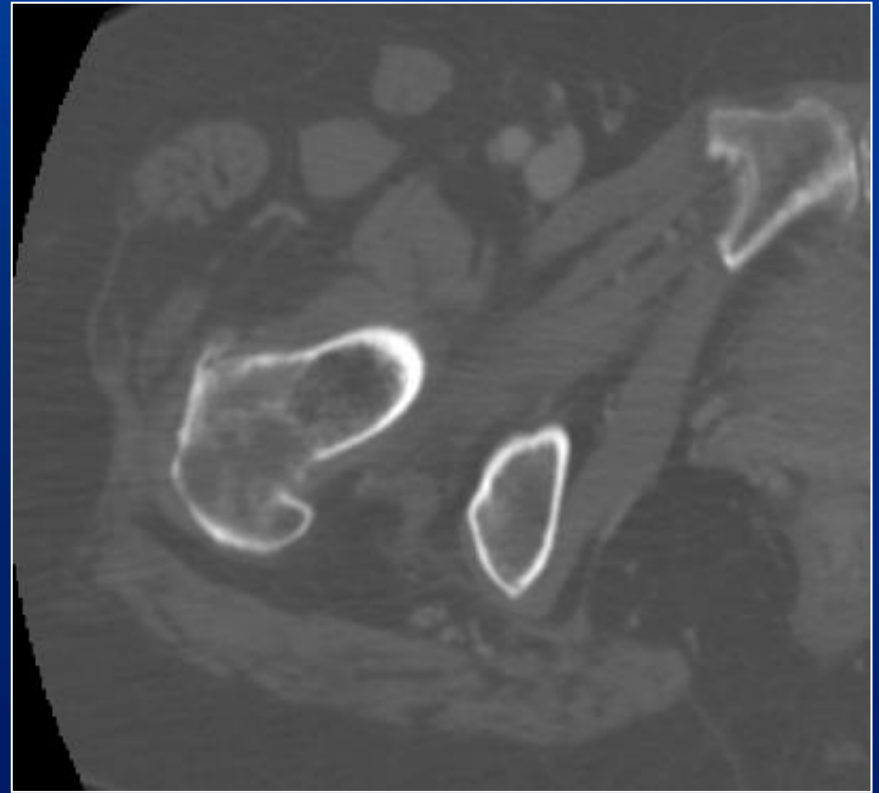


59 anni, Meta Ossee e cerebrali da Ca Renale

Guida Amplioscopica

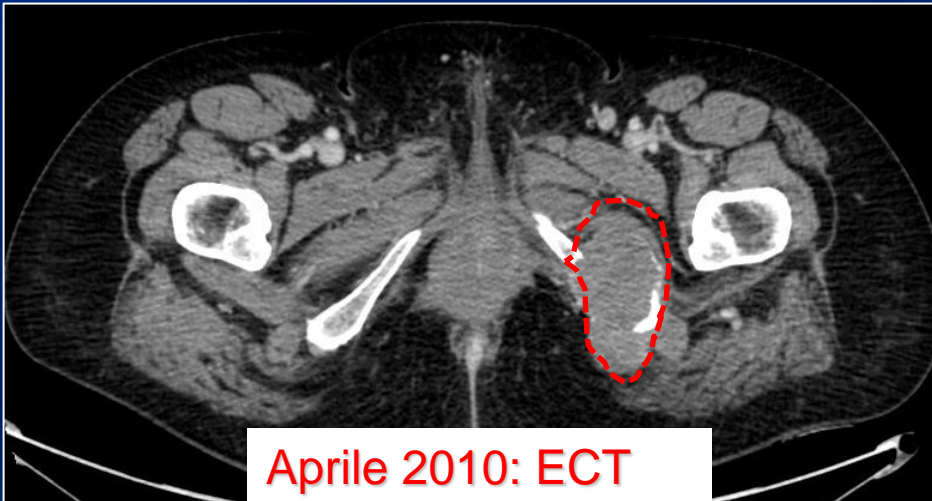


tempo 0



30 giorni

57 anni, Meta Ossee da Ca Renale (già embolizzazione) guida TAC



Aprile 2010: ECT

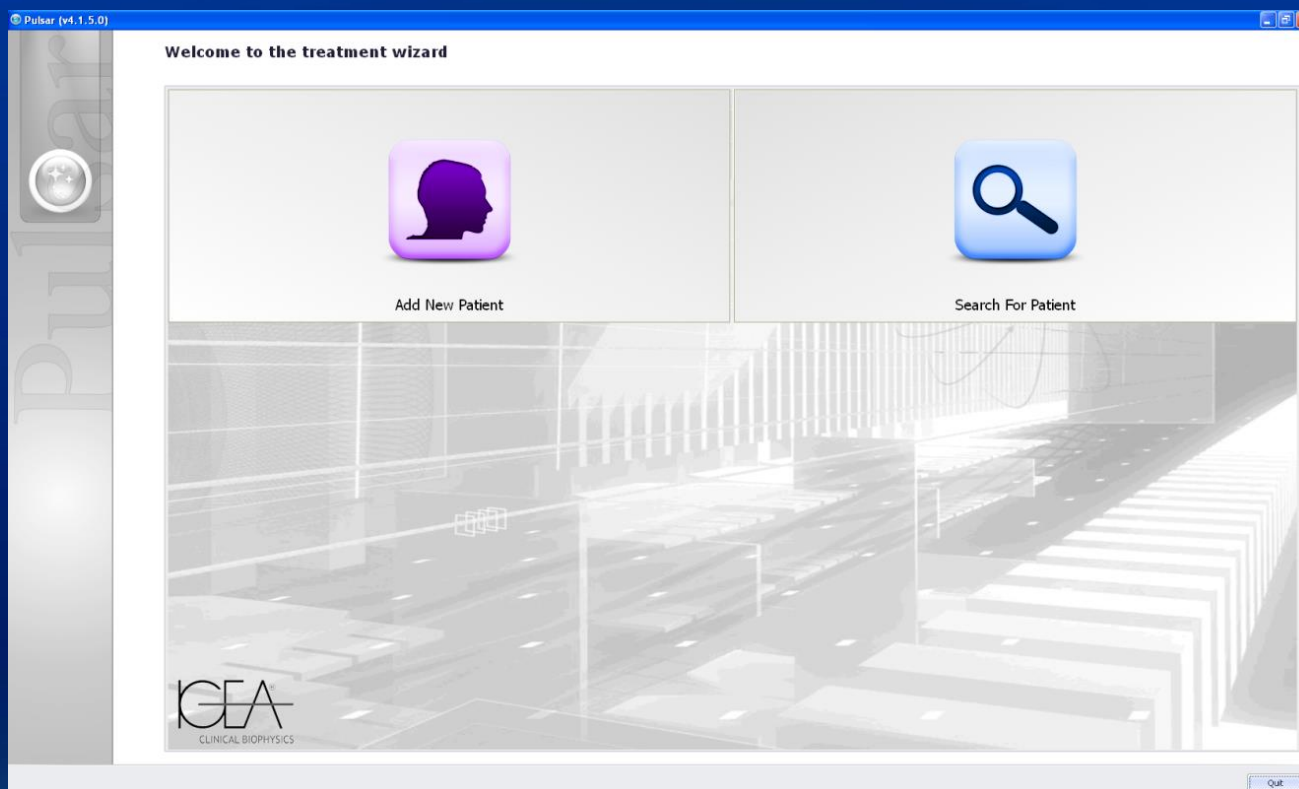


Agosto 2010

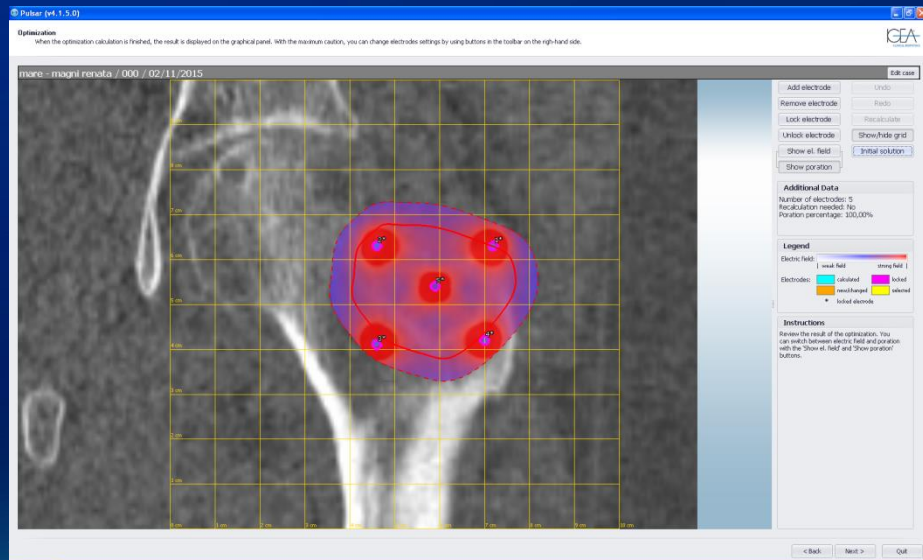
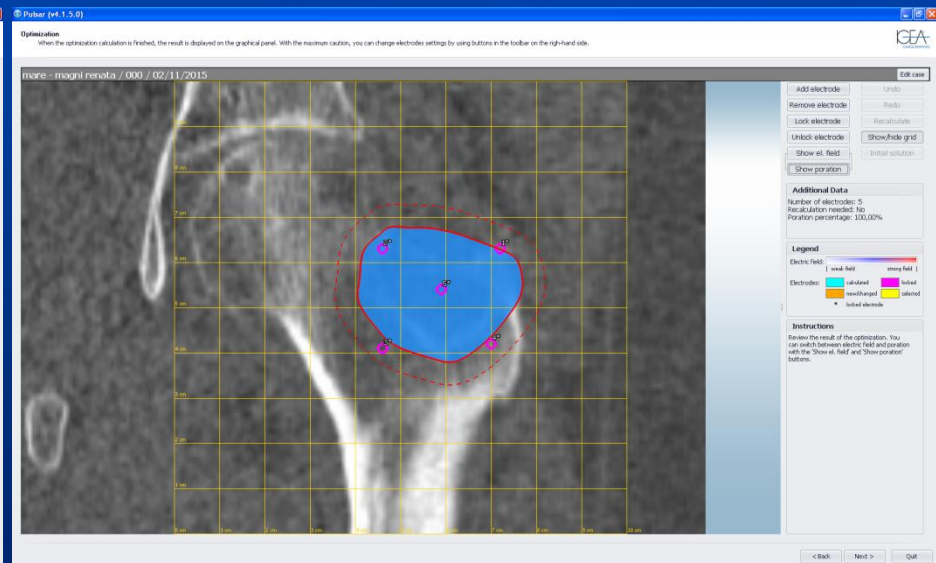
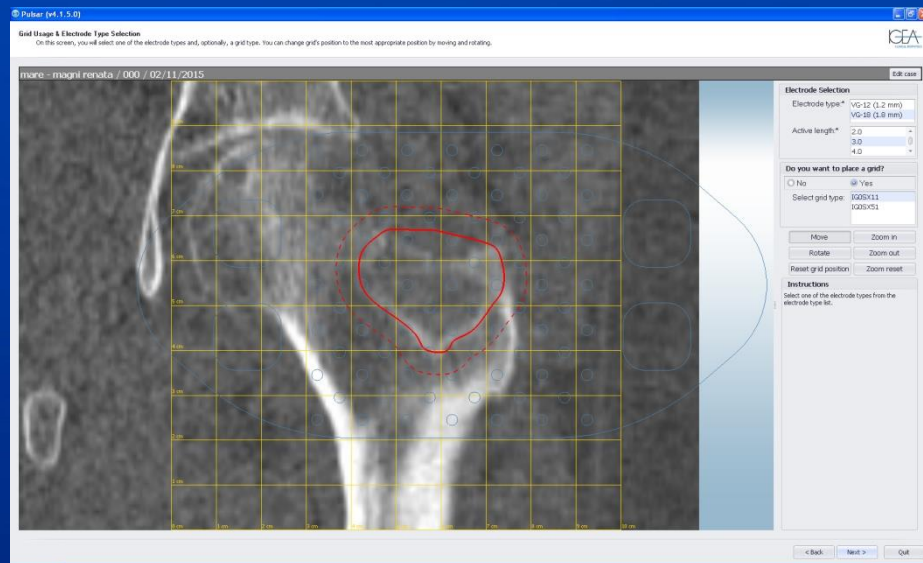
ECT: dolore da 7 a 0

PIANIFICAZIONE (Software Pulsar)

- Salvata sul software, può essere recuperata
- Può essere salvata su USB e caricata sul Cliniporator

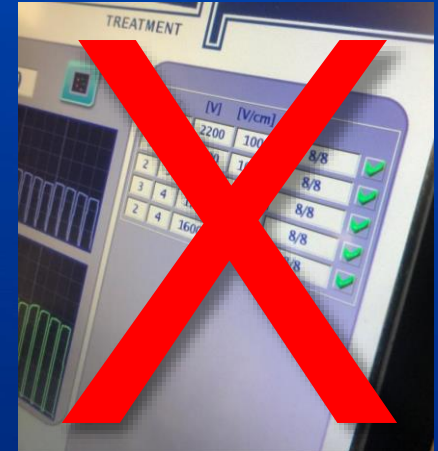


79 anni, meta da Ca Tiroide – già eseguito radio-iodio



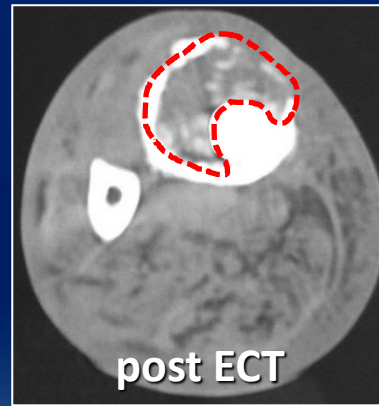
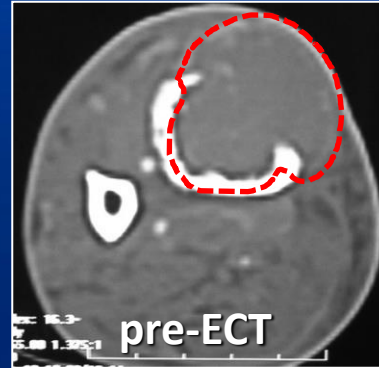
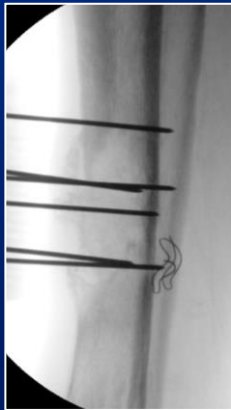
Mezzi di sintesi metallici: problemi conduttività

73 aa, Ca Vescica *pregressa osteosintesi*



- **Necessità di sintesi (preventiva o per frattura patologica), > per istotipi poco sensibili alla radioterapia (comunque possibile, se necessaria, secondariamente)**

75 anni, Meta Osso (fratt patologica), linfonodi, vagina da Ca Colon



2 mesi dopo ECT

19 anni, metastasi da Ca Rene – frattura patologica ECT + CHIODO



Pre-ECT



Post ECT

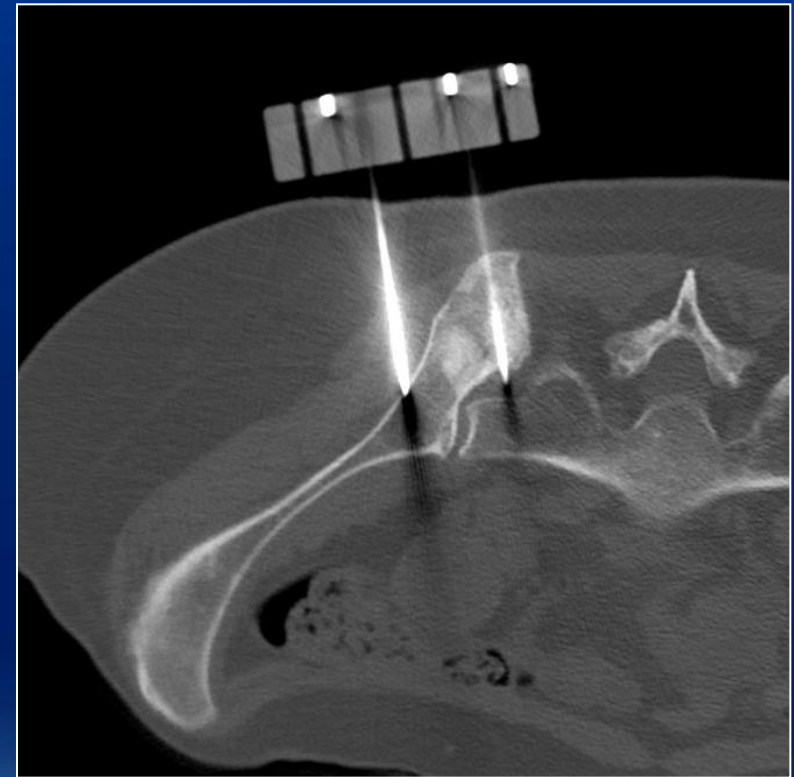
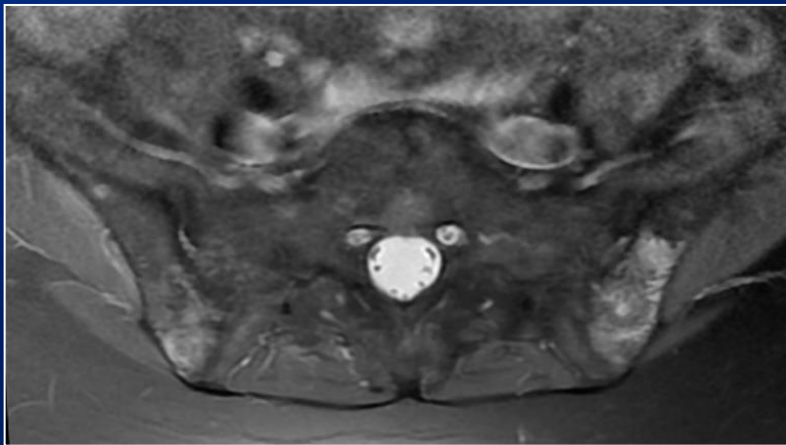
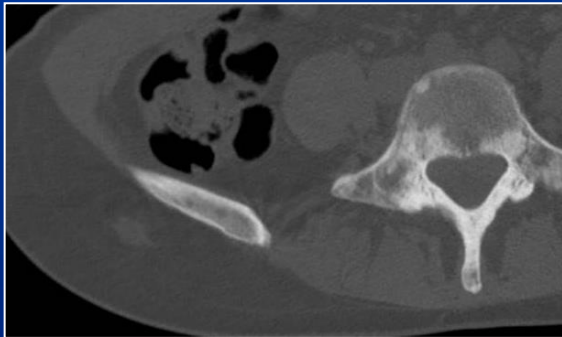


2 anni

- **Pregressi trattamenti locali inefficaci**

**49 anni, Meta Disseminate da Ca Mammella. Terapia sistemica. già RTE
dolore 9/10 SIPS**

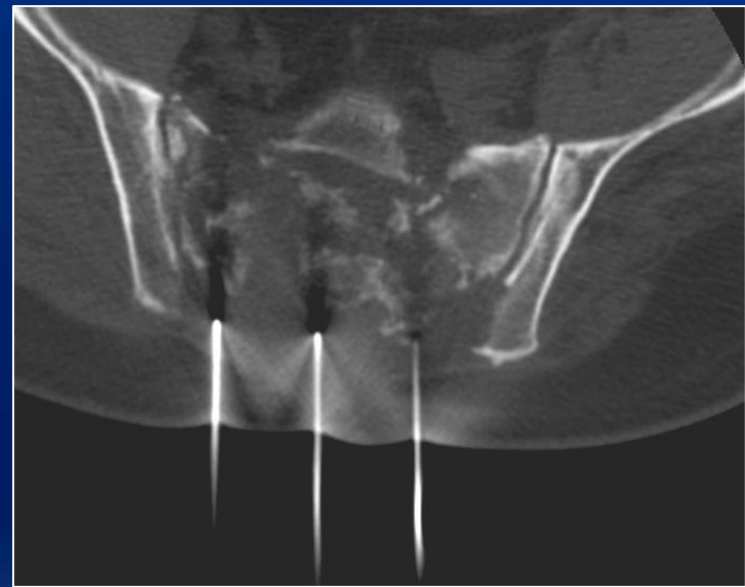
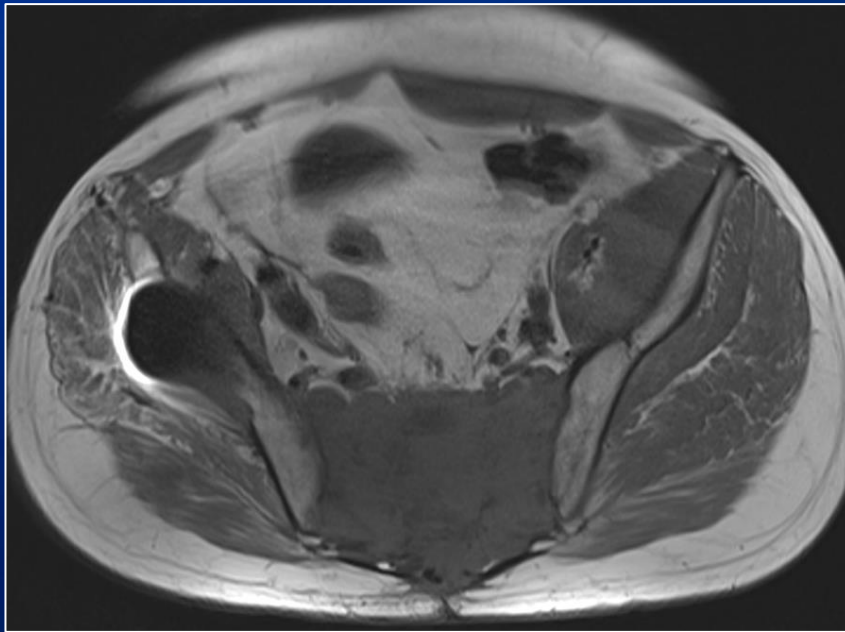
ECT: dolore da 9 a 0



- **Pregressi trattamenti locali inefficaci**

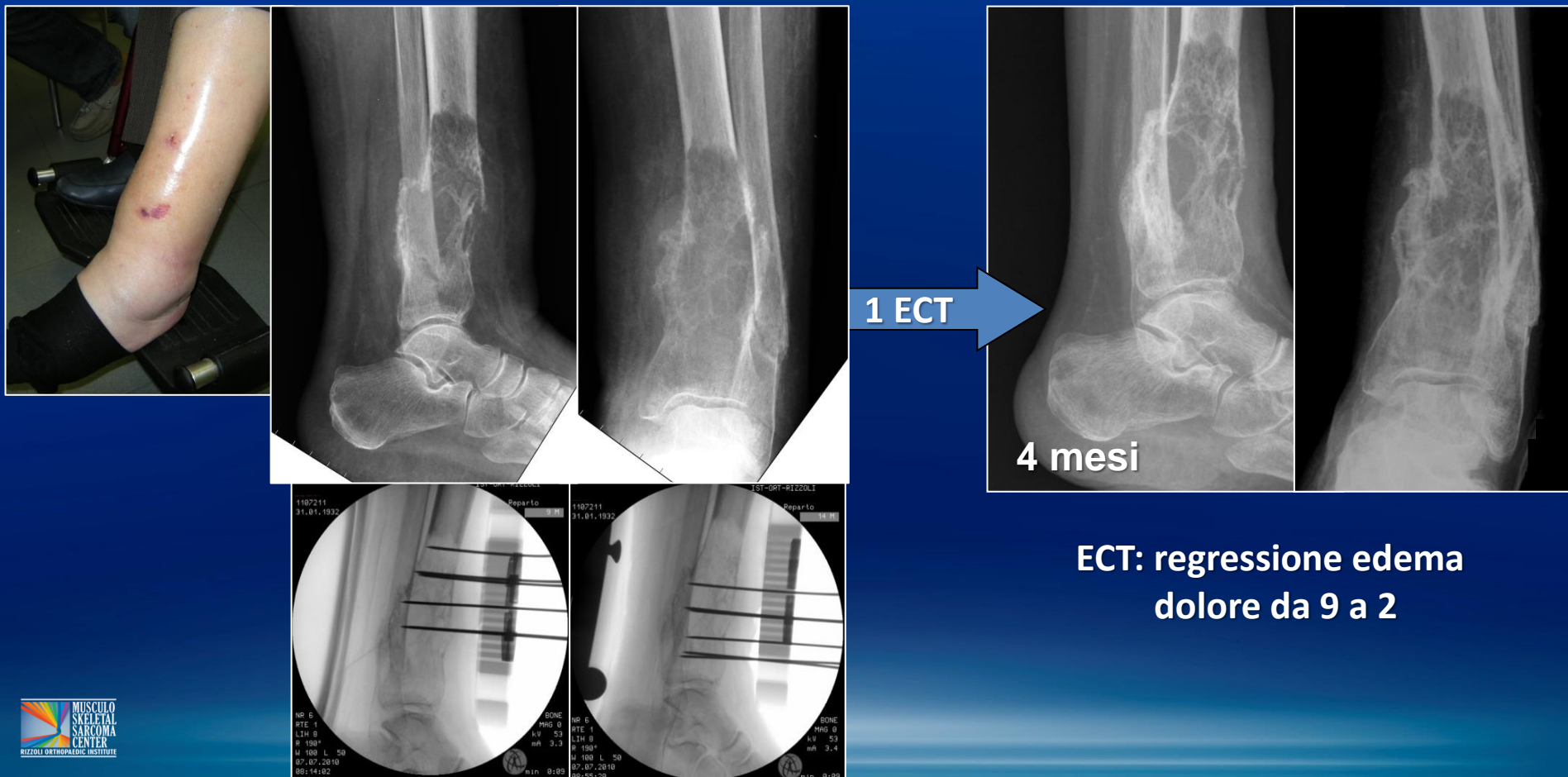
45 anni, Meta Disseminate da Sarcoma dell'Osso Indifferenziato
Terapia sistemica, già RTE + embolizzazione + termoablazione
Dolore 9/10

ECT: dolore da 9 a 2



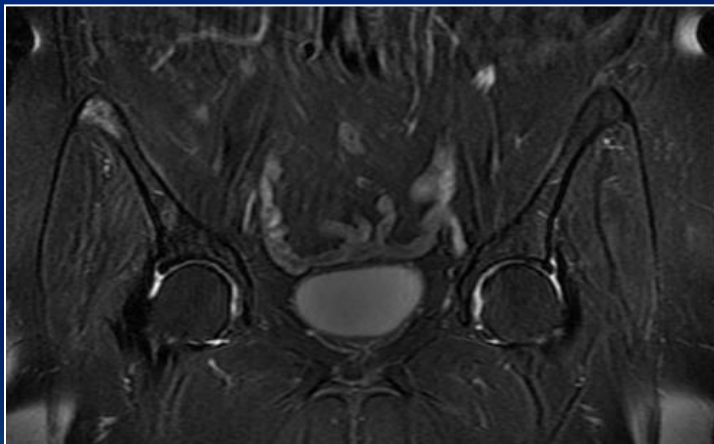
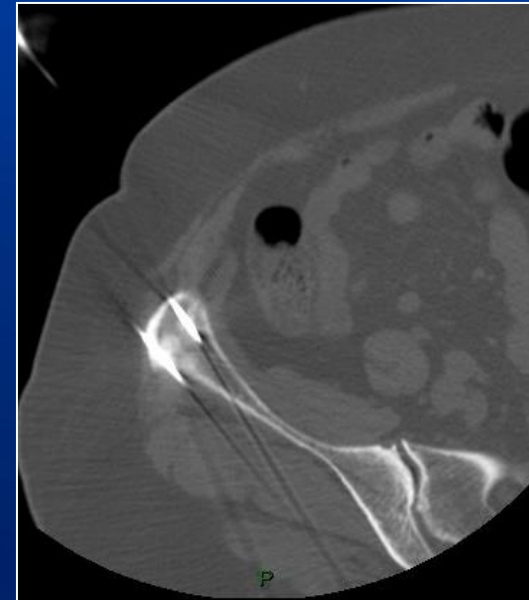
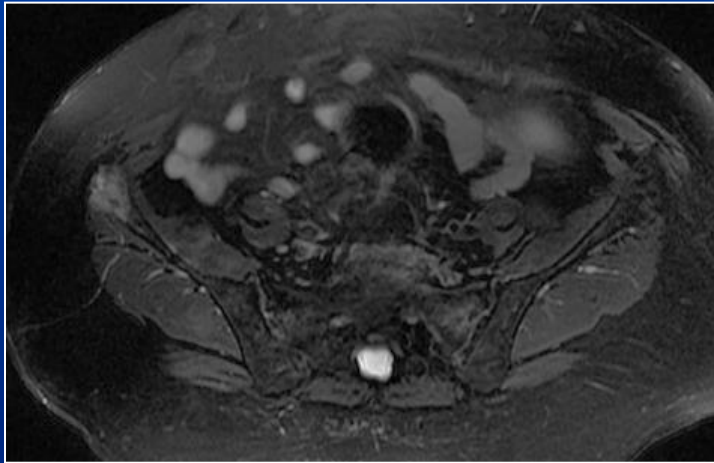
- Migliorare controllo del dolore e Qualità della Vita
- Co-morbidità (controindicazioni alla chirurgia)

**78 anni, Fratt Patol + meta diffuse a ossa, polmmoni, encefalo da Ca Renale.
Edema, impotenza funzionale, dolore 9/10**



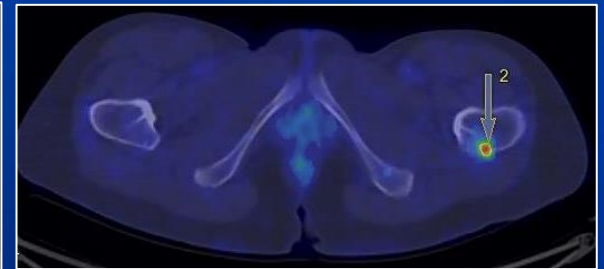
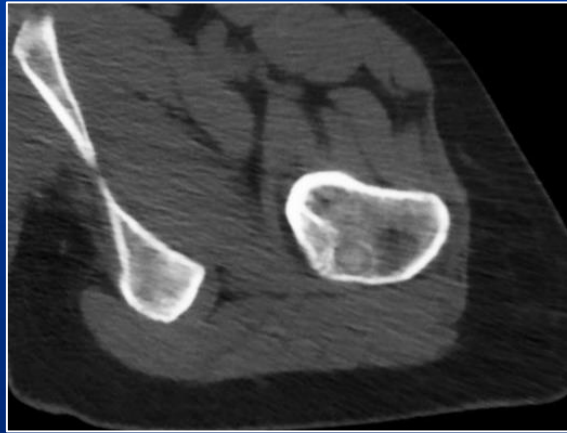
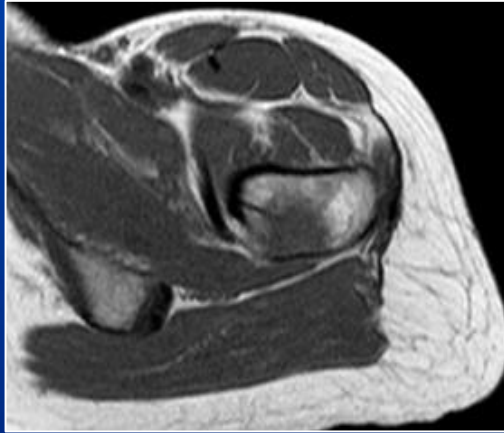
- **Dimensioni**

Copertura complete della lesione

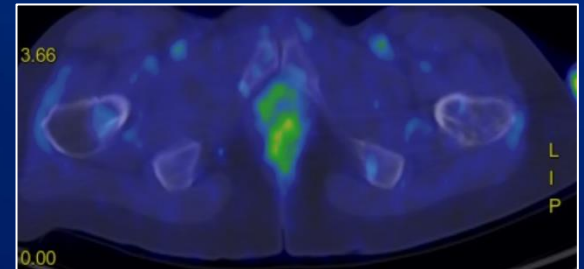
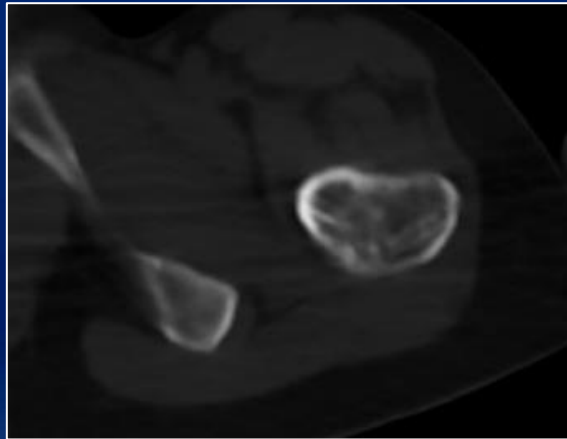
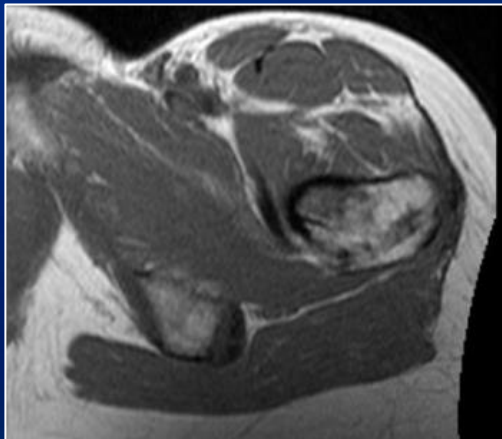


- **Trattamento «Curativo»: lesioni Piccole, Metacrone**

47 years, Endometrial Ca proximal femur – CT guided



Pre-ECT

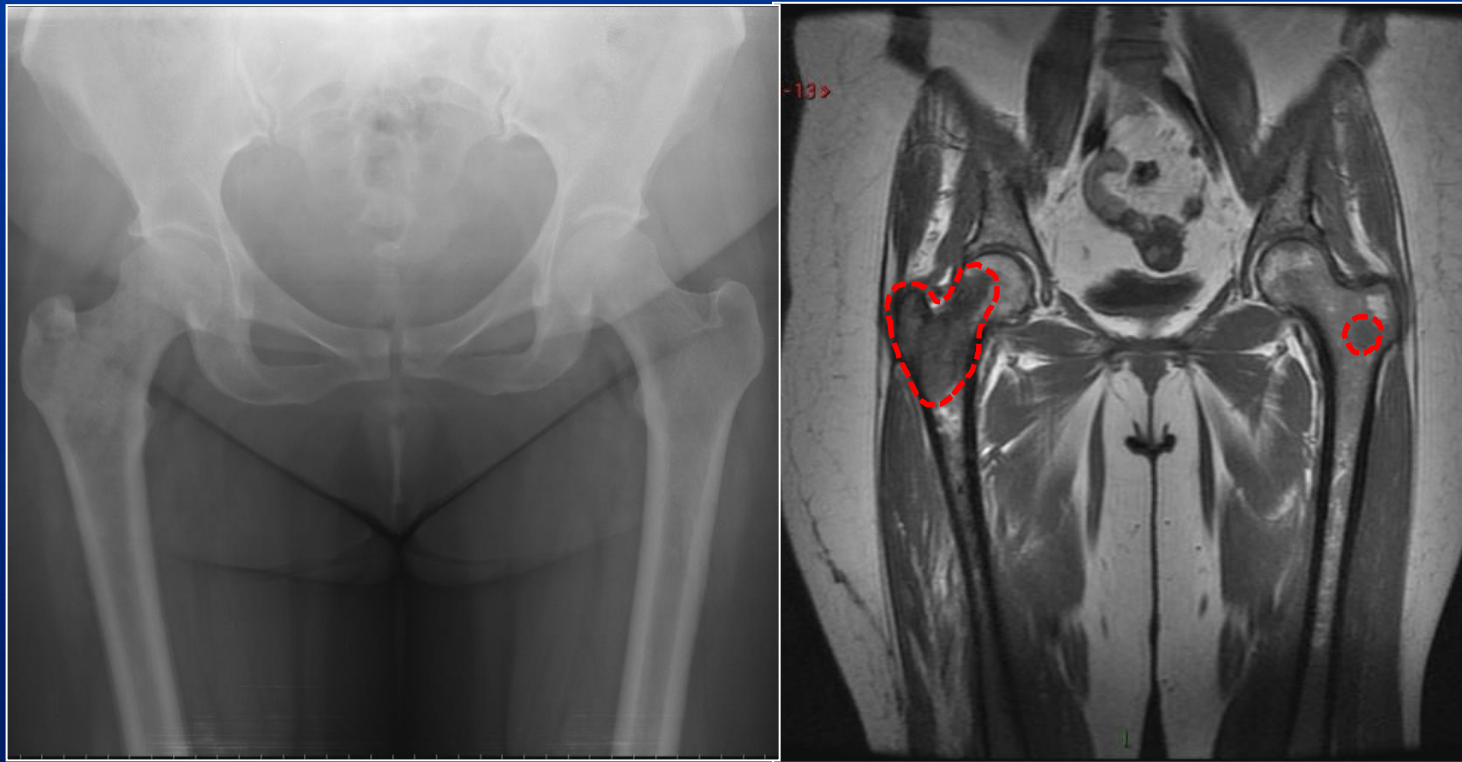


Post-ECT (2 anni)

- Associazione diversi trattamenti locali

Chirurgia

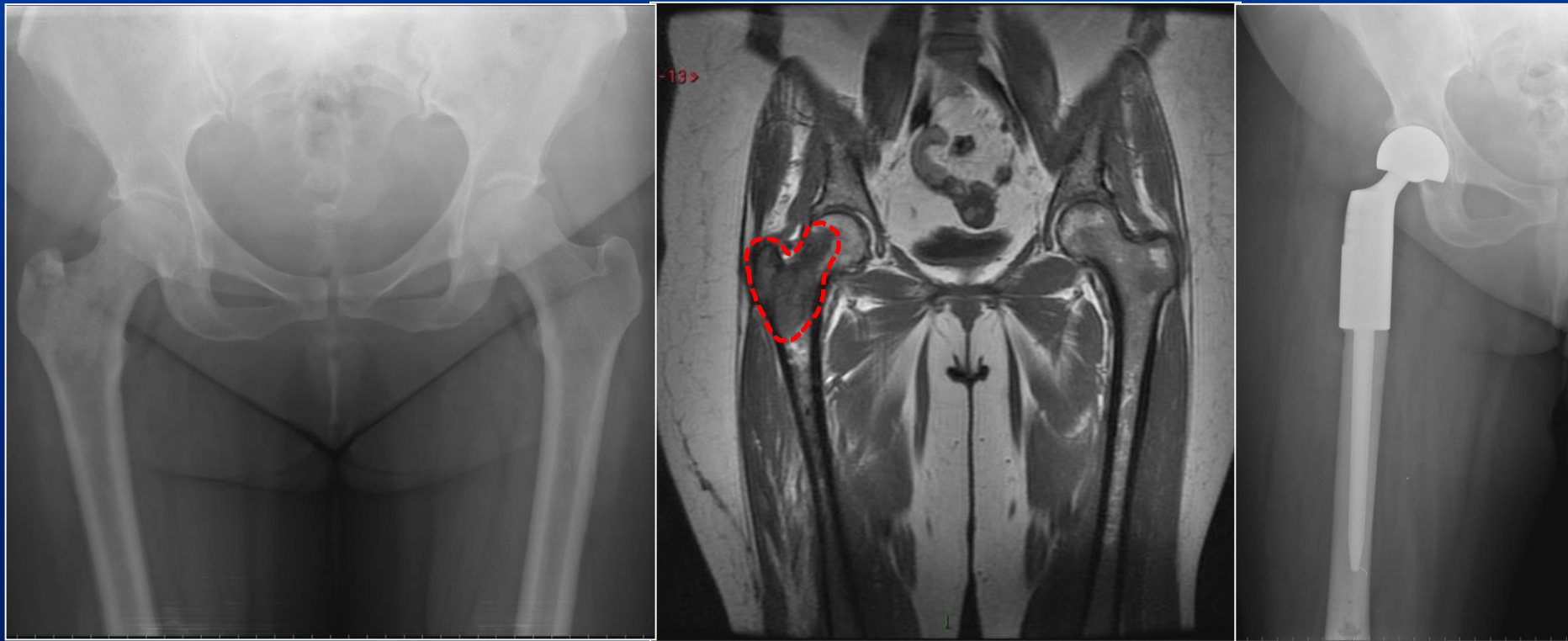
48 anni, Meta Ossee da Carcinoma Mammario



- Associazione diversi trattamenti locali

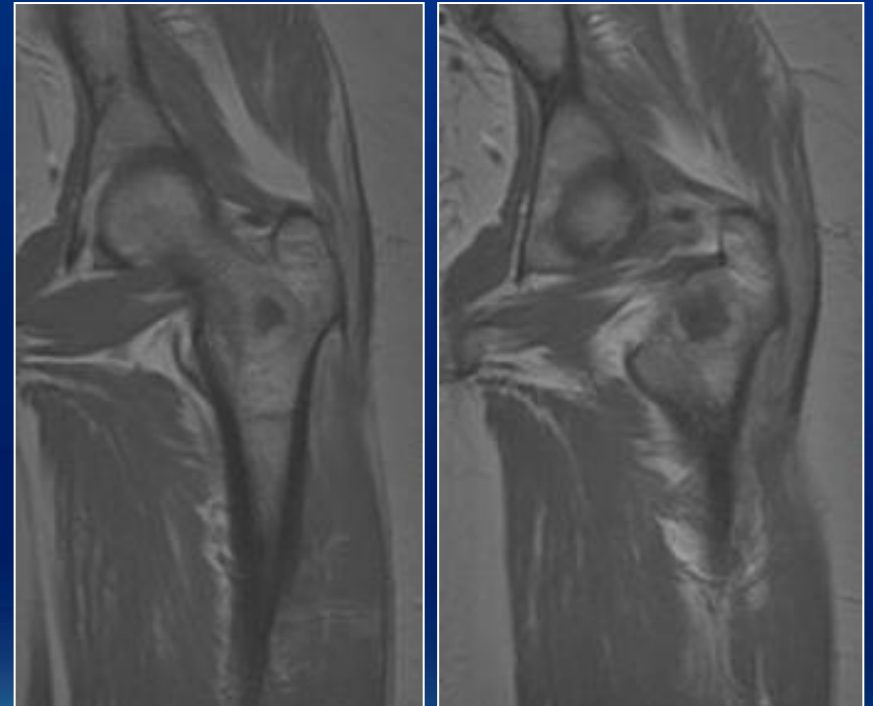
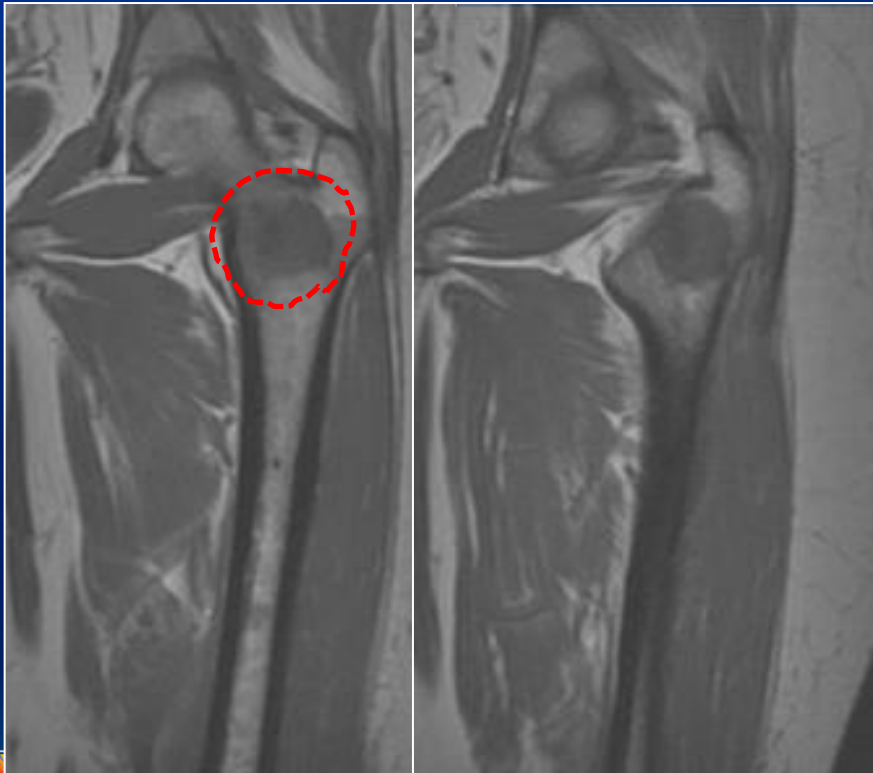
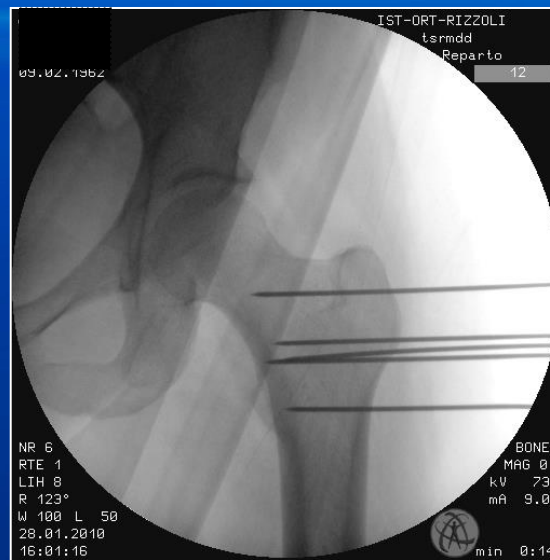
Chirurgia

48 anni, Meta Ossee da Carcinoma Mammario



Dic 2009: Resezione e Protesi Modulare
Femore Proximale dx

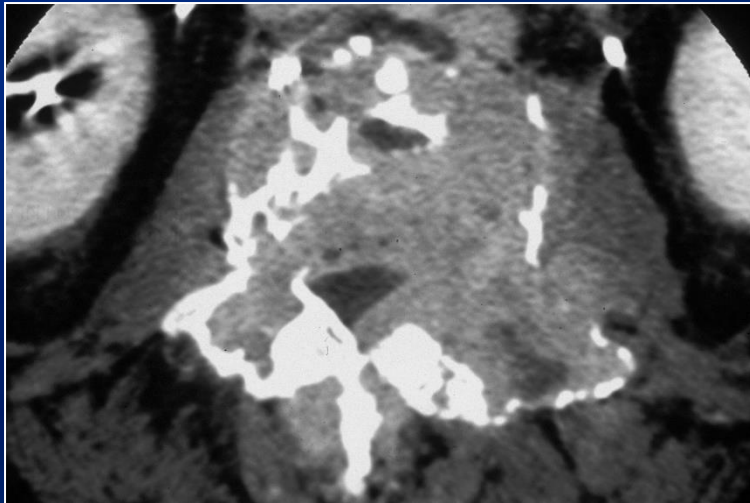
Genn 2010: ECT



5 sett post I ECT

Vertebre

- Difficoltà parallelismo elettrodi
- Vicinanza strutture nervose
- Elettrodi «dedicati»



Feasibility of Electroporation in Bone and in the Surrounding Clinically Relevant Structures: A Preclinical Investigation

Technology in Cancer Research & Treatment
2016, Vol. 15(6) 737–748
© The Author(s) 2015
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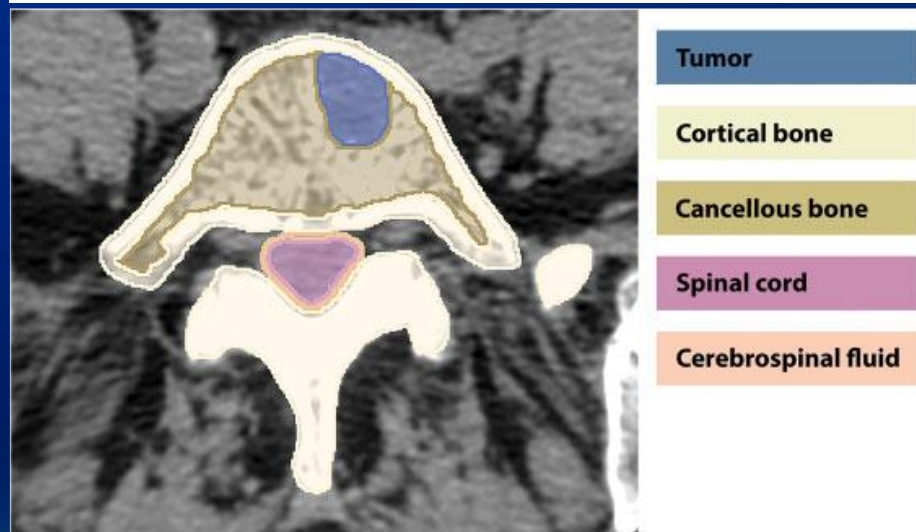
2016

Matilde Tschon, PhD^{1,2}, Francesca Salamanna, PhD²,
Mattia Ronchetti, BSc³, Francesco Cavani, BSc⁴,
Alessandro Gasbarrini, MD⁵, Stefano Boriani, MD⁵,
and Milena Fini, MD^{1,2}

Electrochemotherapy of Spinal Metastases Using Transpedicular Approach—A Numerical Feasibility Study

Helena Cindrič, BSc¹, Bor Kos, PhD¹, Giuseppe Tedesco, MD²,
Matteo Cadossi, MD, PhD², Alessandro Gasbarrini, MD²,
and Damijan Miklavčič, PhD¹

2018

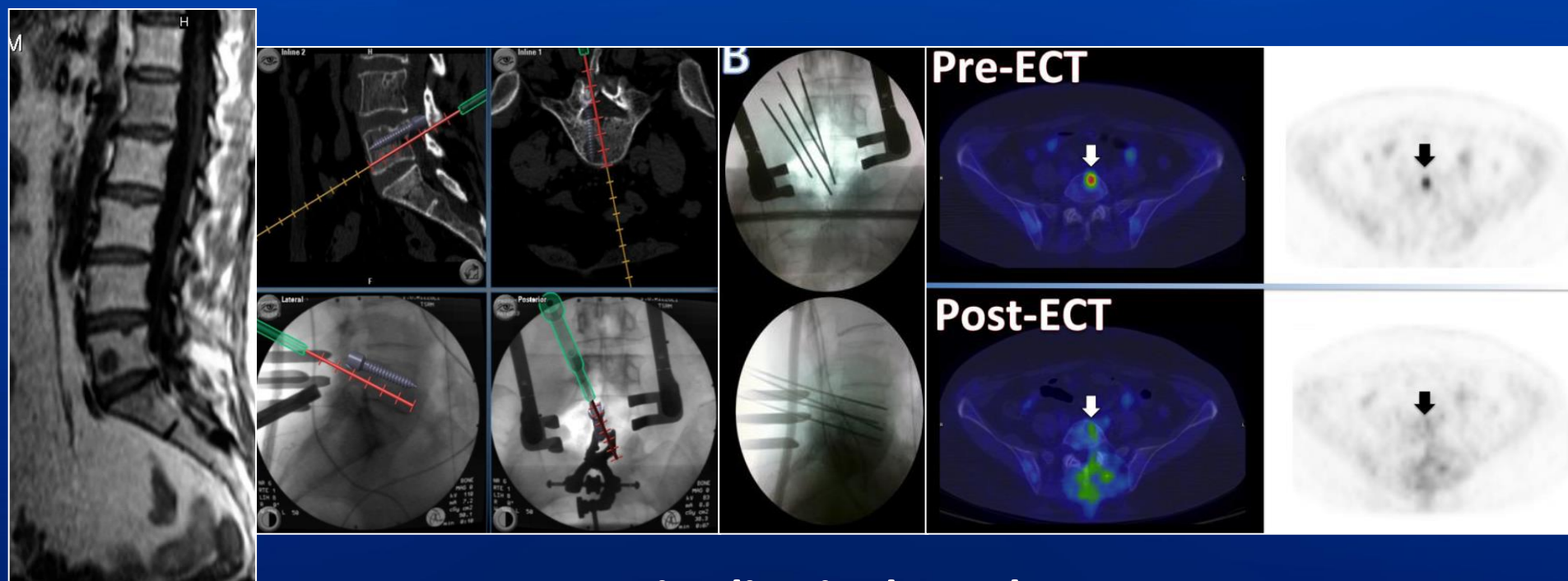


2015

Spine (Phila Pa 1976). 2015 Dec;40(24):E1340-6

ELECTROCHEMOTHERAPY TO METASTATIC SPINAL MELANOMA: A NOVEL TREATMENT OF SPINAL METASTASIS?

[Gasbarrini A](#)¹, [Campos WK](#), [Campanacci L](#), [Boriani S](#).



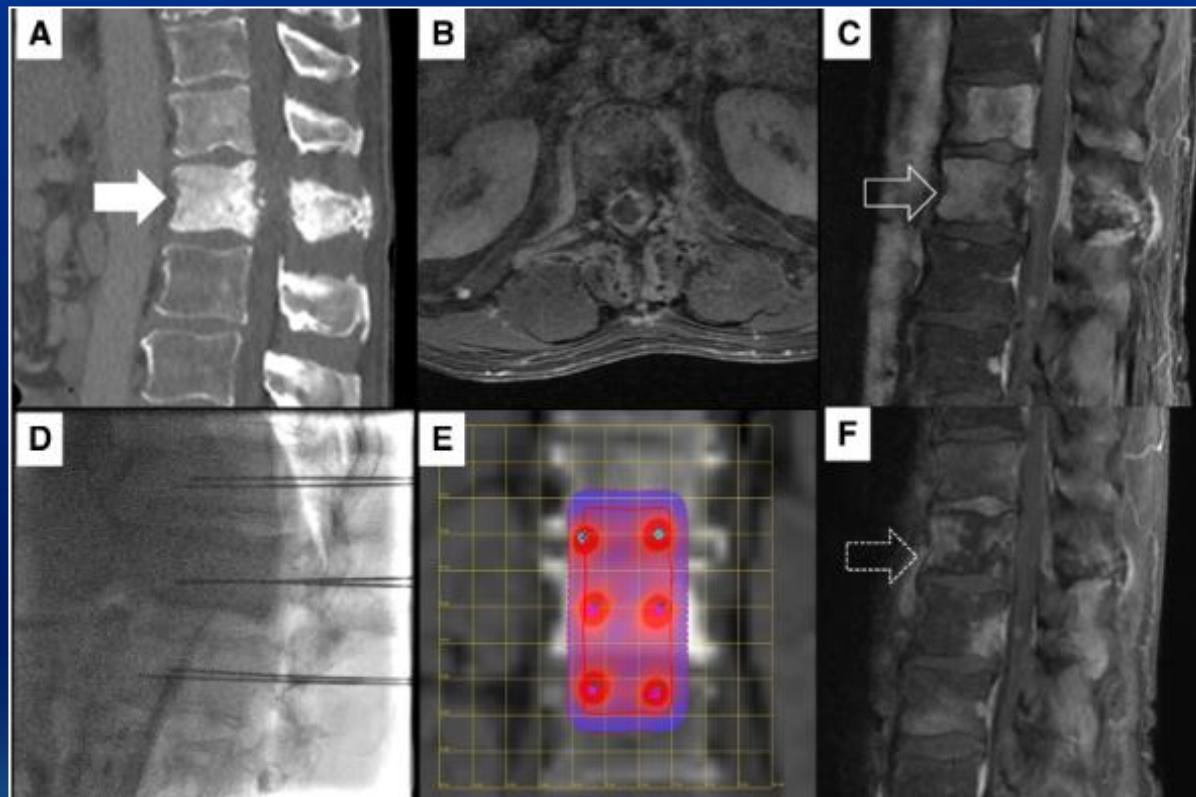
- **Metastasi solitaria da Melanoma**
- **L5**
- **A cielo aperto**
- **Inserimento elettrodi NAVIGATO**



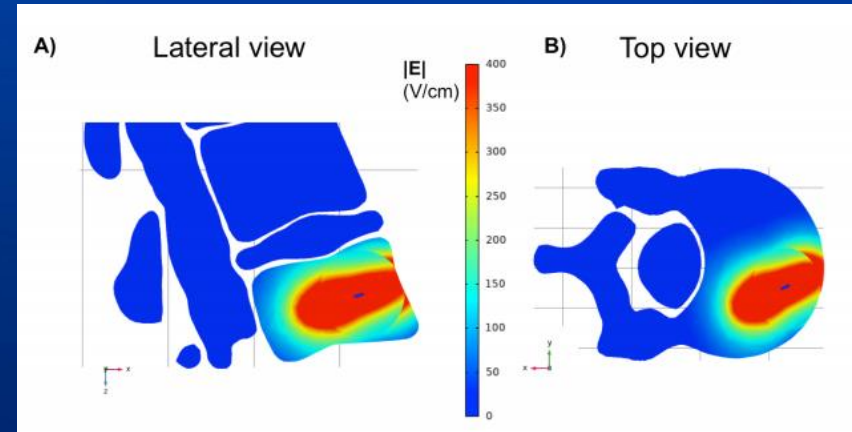
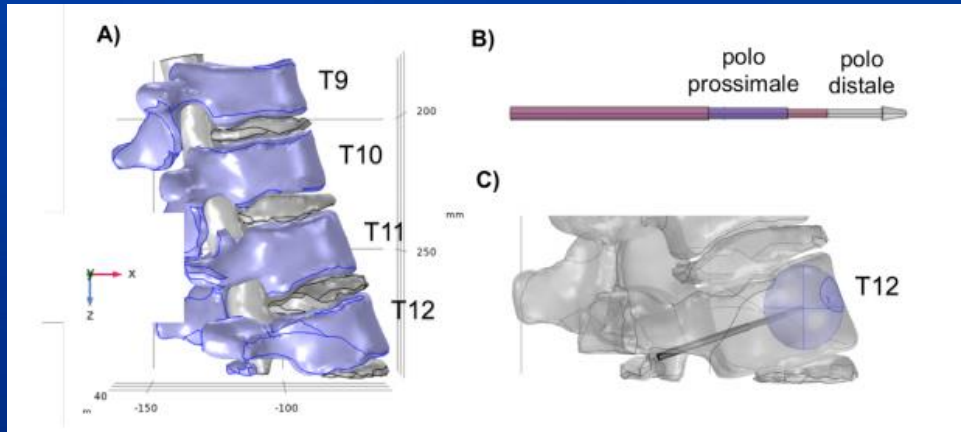
CASE REPORT

Percutaneous Image-Guided Electrochemotherapy of Spine Metastases: Initial Experience

François H. Cornelis¹ · Mohamed Ben Ammar¹ · Maud Nouri-Neuville¹ ·
Lise Matton² · Marc Antoine Benderra³ · Joseph Gligorov³ · Vincent Fallet² ·
Luis M. Mir⁴



Elettrodi Bipolari



Progetto di Ricerca “Elettrodi Bipolari Assiali e sviluppo di Software per la Pianificazione Preoperatoria per il Trattamento delle Metastasi Vertebrali con Elettrochemioterapia” (Rizzoli: Chirurgia Sperimentale-Ortopedia Oncologica)

Selezione dei Pazienti

Approccio Multidisciplinare

Istotipo (risposta al trattamento sistemico)

Sede, Dimensioni, Sintomi

Valutazione dei tempi di Ri-Trattamento

Associazione con altre terapie

Sviluppo della Tecnologia (es. Elettrodi per Vertebre)



Necessità di adeguato protocollo terapeutico

REGISTRO dei PAZIENTI TRATTATI con ECT per METASTASI OSSEE

PROGETTO REINBONE



- **Settembre 2014**
 - ✓ Registro di pazienti affetti da Metastasi Ossee trattati con Elettrochemioterapia
 - ✓ Approvazione del Comitato Etico del Rizzoli (Bologna)
- **11 Centri**
- **120 pazienti ad oggi**

Maggio 2021



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Operating procedures for electrochemotherapy in bone metastases: Results from a multicenter prospective study on 102 patients

Laura Campanacci ^{a,*}, Giuseppe Bianchi ^a, Luca Cevolani ^a, Costantino Errani ^a,
Giovanni Ciani ^a, Giancarlo Facchini ^b, Paolo Spinnato ^b, Andrea Tognù ^c, Leo Massari ^d,
Francois H. Cornelis ^e, Mario Mosconi ^g, Daniele Screpis ^h, Francesco Benazzo ⁱ,
Barbara Rossi ^j, Enrico Bonicoli ^k, Flavio Fazioli ^l, Mario Nicolosi ^m, Michele Boffano ⁿ,
Raimondo Piana ⁿ, Francesca De Terlizzi ^o, Matteo Cadossi ^o, Davide Maria Donati ^a

- 102 pazienti (105 trattamenti)
- Marzo 2014 - febb 2020
- Valutazione Clinica e Radiologica a 60 - 90 giorni - 6 mesi

PROGETTO REINBONE



CENTERS	# PATIENTS
BOLOGNA	57
TORINO	20
CATANIA	7
NAPOLI	4
PARIGI	4
FERRARA	3
PAVIA	2
NEGRAR	2
ROMA S.ANDREA	2
PISA	1
TOTAL	102

Rizzoli 2009-2014 : 32 casi

Frattura Patologica (52 pts, 51%)

Meta viscerali (49 pts, 48%)

**ECT+CHIODO: 24 casi (23 IOR,
1 PV)**

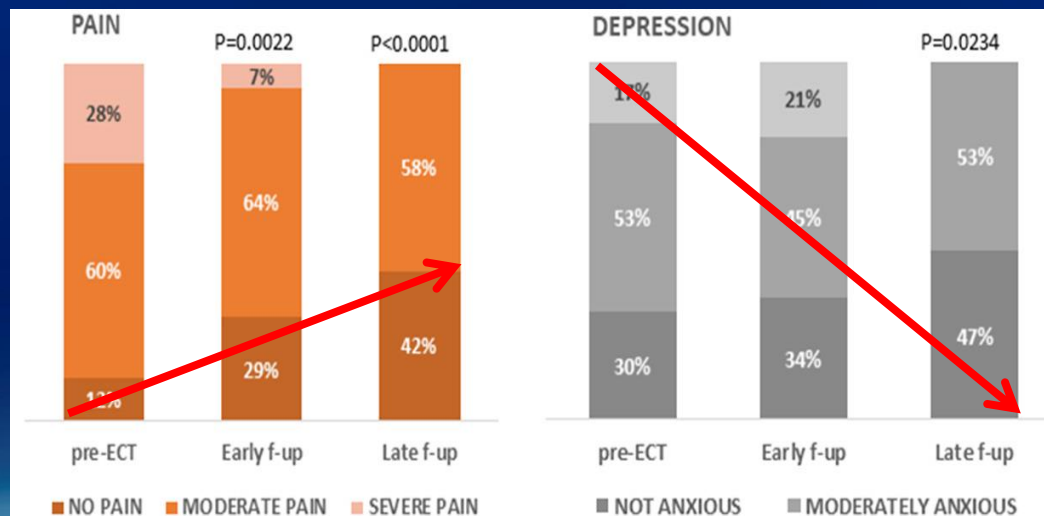
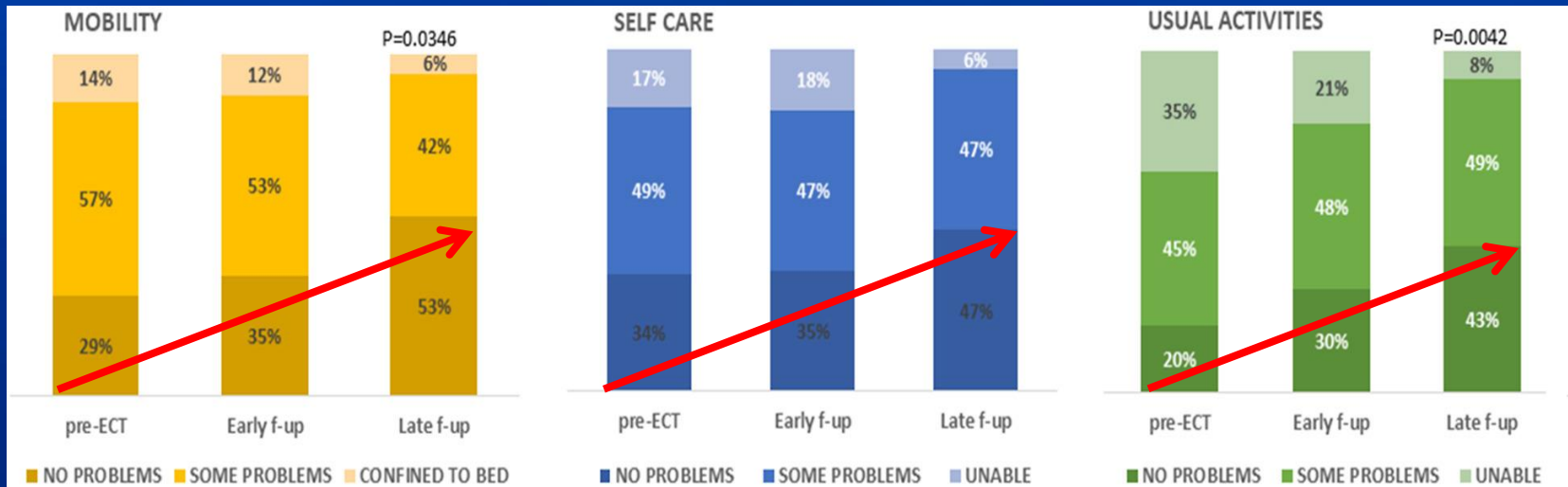
RISPOSTA AL TRATTAMENTO (RECIST+PERCIST)

- Valutabile per 89 pz; 43 con FU > 3 mesi (media 10.7 mesi)

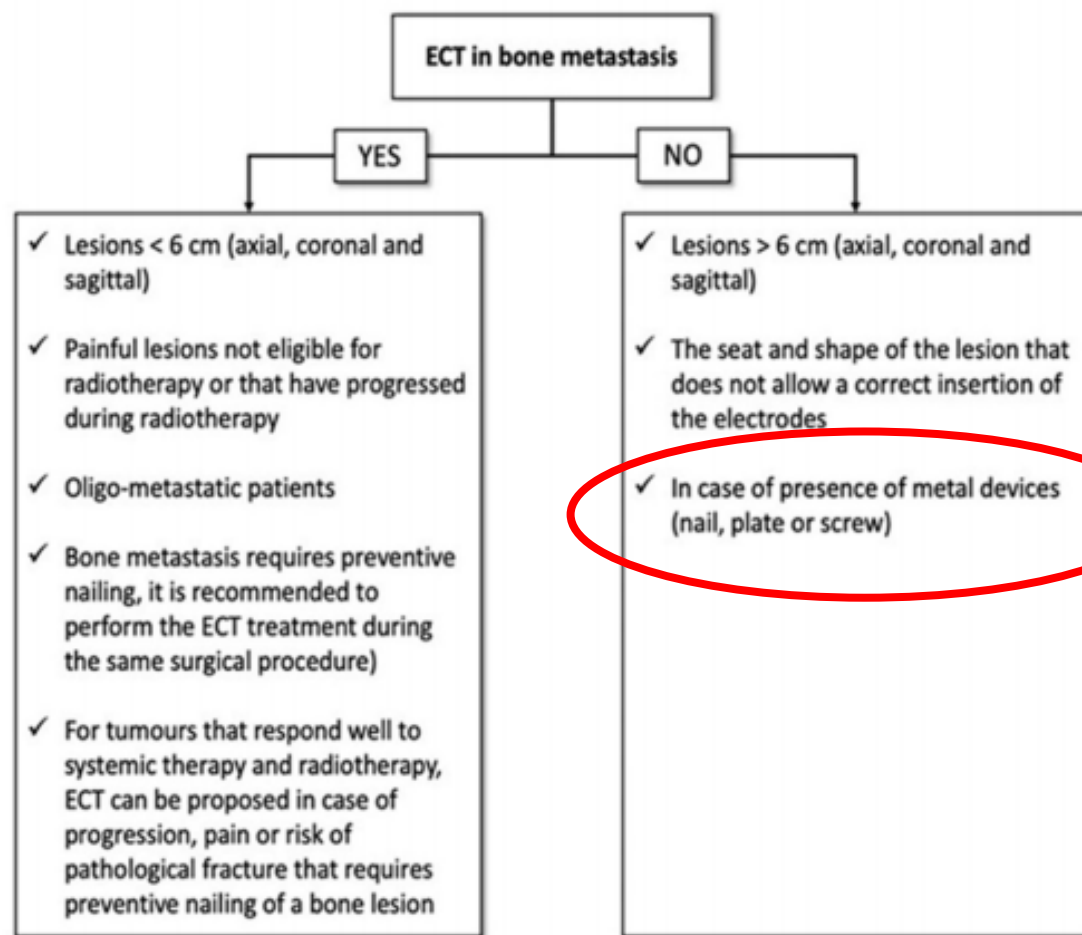
RESPONSE	#PTS (%)	Axial plane Median (range) mm	Coronal plane Median (range) mm	Sagittal plane Median (range) mm	#Completely covered lesions (%)
CR	2 (3%)	22.5 (22-23)	29 (24-34)	30.5 (21-40)	2 out of 2 (100%)
PR	34 (37%)	35 (7-89)	40 (7-85)	35 (7-85)	28 out of 34 (80%)
SD	45 (52%)	44 (10-88)	47 (10-120)	48 (10-120)	31 out of 45 (69%)
PD	8 (8%)	46 (20-140)	62 (37-120)	62 (37-120)	4 out of 8 (50%)

ECT + CHIODO: 24 casi

RISPOSTA AL TRATTAMENTO (RISPOSTA CLINICA)



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**Controindicazioni
Relative**

Fig. 4. Proposed algorithm for indications for ECT in bone metastases.



laura.campanacci@ior.it