The dark side of the guidelines

2nd Interventional Radiologist under 40 Meeting

Interventional Oncology

8-10 Maggio 2017

Bologna

Società Medica Chirurgica - Palazzo dell'Archiginnasio

TRATTAMENTI ABLATIVI: IN QUALI TUMORI?

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Trattamento ablativo: applicazione diretta di terapie fisiche o chimiche in una specifica lesione tumorale per ottenere la sua distruzione

***Ahmed et al.**, Image-guided tumor ablation: standardization of terminology and reporting criteria – a 10-year upodate, Radiology 2014*

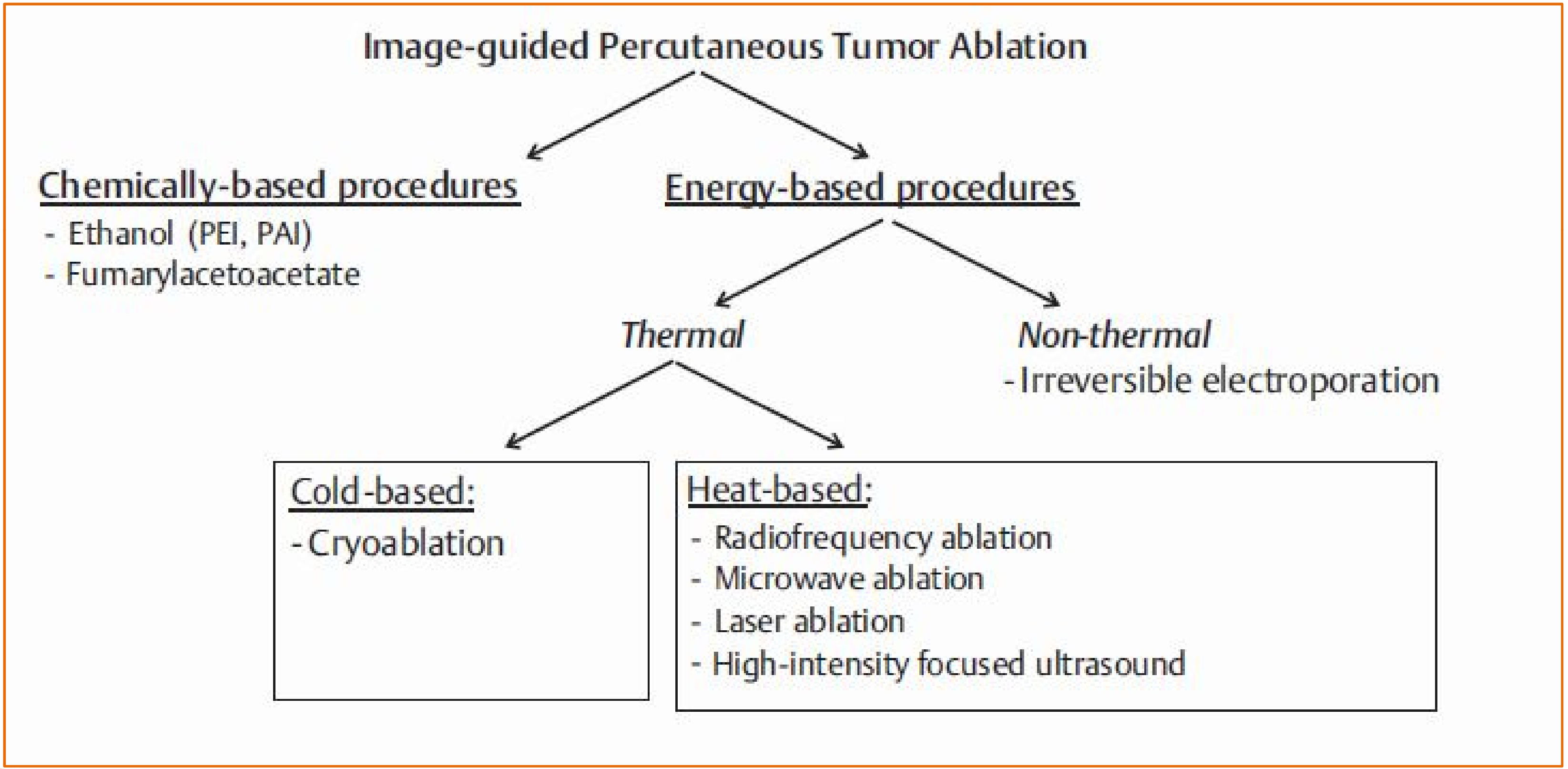


Image-guided Percutaneous Tumor Ablation

Chemically-based procedures
- Ethanol (PEI, PAI)
- Fumarylacetoacetate

Energy-based procedures

Thermal

Cold-based:
- Cryoablation

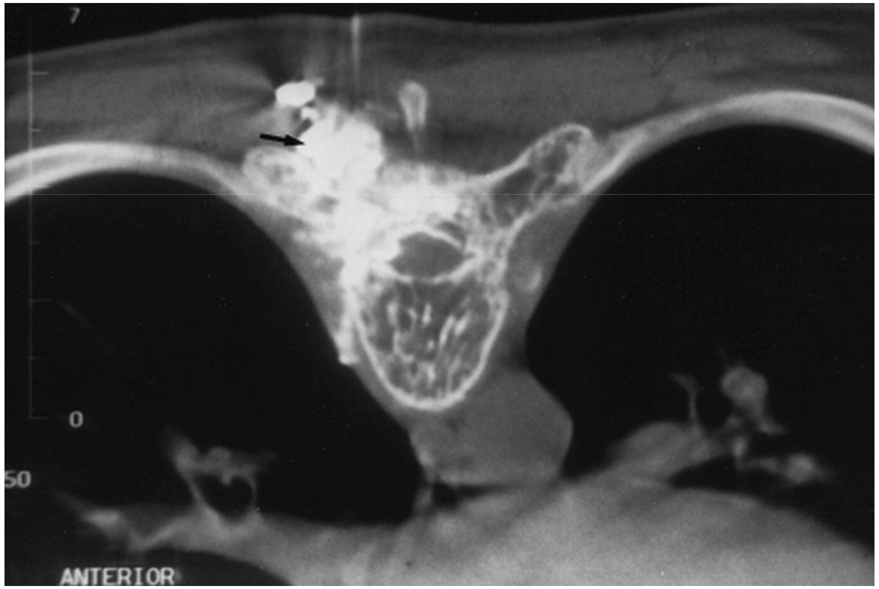
Heat-based:
- Radiofrequency ablation
- Microwave ablation
- Laser ablation
- High-intensity focused ultrasound

Non-thermal
- Irreversible electroporation

***Ringe at al.**, Thermoablation of bone tumors, Fortschr Rontgenstr 2015*

ALCOL

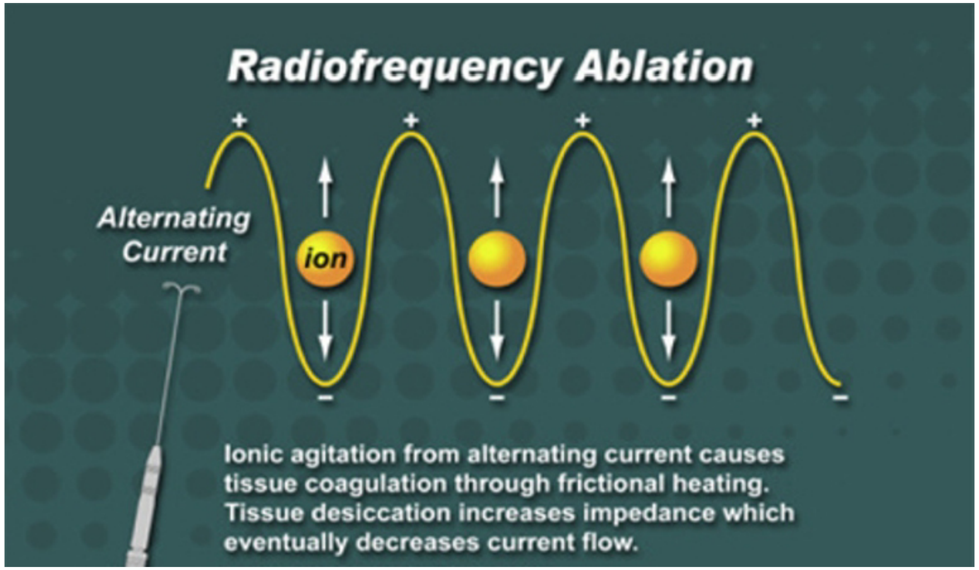
- Azione diretta (disidratazione cellulare) ed indiretta (trombosi vascolare)
- Basso costo
- Dimensioni e configurazione della zona di ablazione scarsamente prevedibile e riproducibile



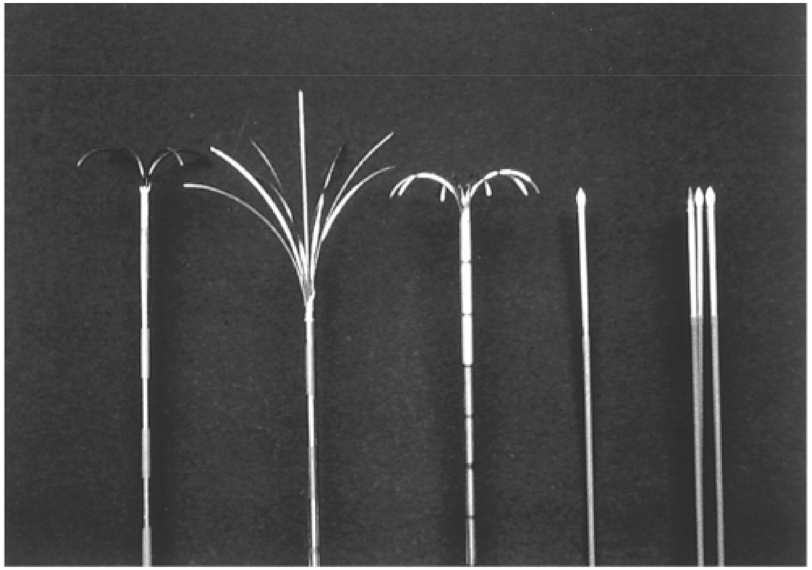
Gangi et al., *Percutaneous bone tumor management, Semin Intervent Radiol 2010*
Gabal et al., *Percutaneous technique for sclerotherapy of vertebral hemangioma compressing spinal cord, Cardiovasc Interv Radiol 2002*

RFA

- Corrente alternata (375-600kHz) tramite elettrodi 14-17G
- Denaturazione proteica e necrosi coagulativa tra 60-100°C
- Carbonizzazione e vaporizzazione tissutale >100°C
- Differenti tipi di elettrodi (unipolari, bipolari, ad «ombrello», con sistema di raffreddamento, navigazionali)
- Contro: non visualizzazione dei margini di ablazione, impedenza tissutale, maggiore dolore peri- e post-procedurale, effetto sifone vicino a vasi >3mm



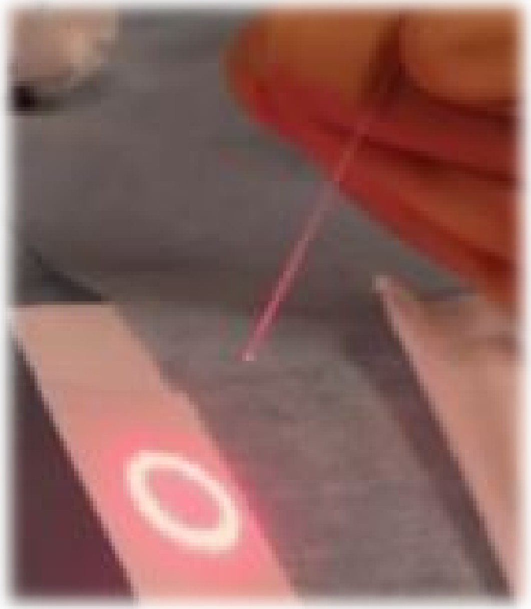
Ionic agitation from alternating current causes tissue coagulation through frictional heating. Tissue desiccation increases impedance which eventually decreases current flow.



Rybak et al., *Fire and ice: thermal ablation of musculoskeletal tumors, Radiol Clin North Am 2009*

LASER

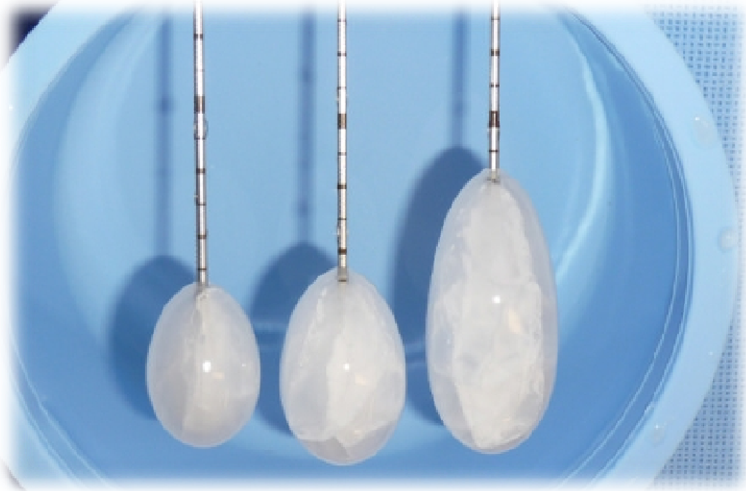
- Fibre ottiche che trasmettono luce infrarossa (800-1000 nm)
- Energia: [dimensioni (mm) x 100 J + 200 J]
- Tempo: 200-600 secondi
- Vantaggi: dimensione della zona di ablazione prevedibile, no interazione con PMK/ICD, basso costo
- Compatibilità RM
- Area di ablazione relativamente piccola (fino a 1.6cm)

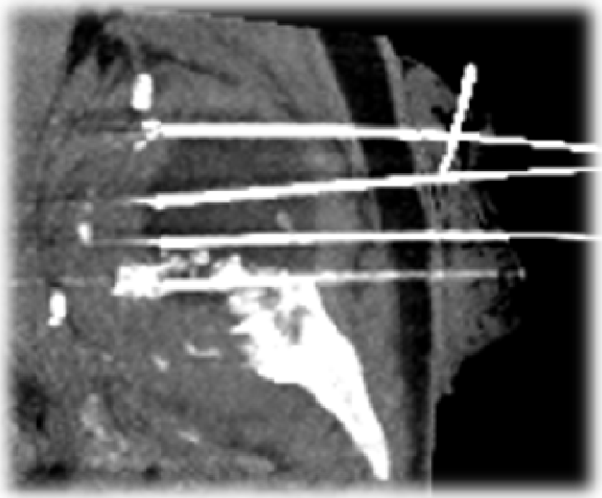


Tsoumakidou et al., *Percutaneous image-guided laser photocoagulation of spinal osteoid osteoma: a single-institution series, Radiology 2016*
Gangi et al., *Osteoid osteoma: percutaneous laser ablation and follow-up in 114 patients, Radiology 2007*

CRIO

- Raffreddamento della criosonda (11-17G) tramite espansione di Argon (effetto Joule-Thompson) e successivo scongelamento tramite Elio
- Temperature >-20-40°C sono necessarie per una completa morte cellulare
- Tipico protocollo: 2 cicli di congelamento-scongelamento attivo (10-5-10 min)
- Vantaggio rispetto alla RF nel trattamento di lesioni osteoaddensanti
- Visualizzazione dell’ice-ball con la finestra dei tessuti molli a 400HUW-40HUL (necrosi cellulare a circa 3-5mm dal margine esterno)
- Ridotto dolore peri-e post-procedurale (effetto analgesico intrinseco)
- Possibilità di trattare grandi volumi (fino a 25 sonde in differenti direzioni)
- Procedura più costosa, tempi procedurali più lunghi

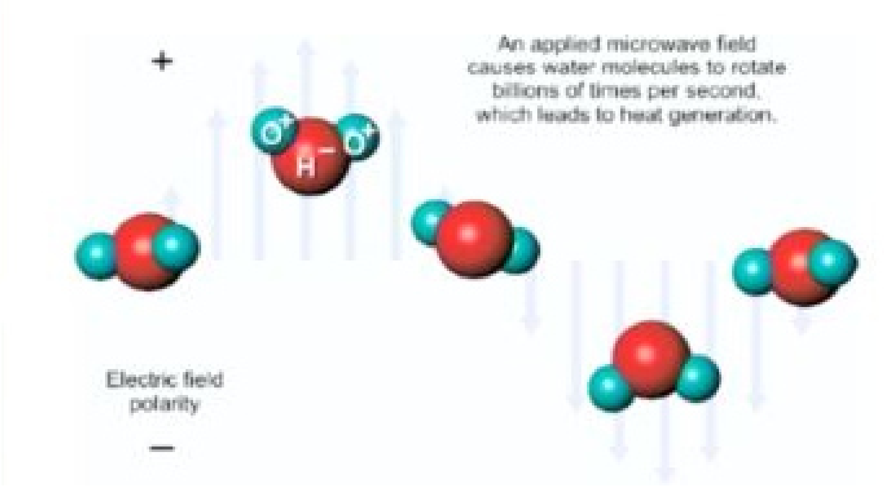




Barile et al., Minimally invasive treatments of painful bone lesions, state of the art, Med Oncol 2017
Tomasian et al., Percutaneous ablation in painful bone tumors, Sem Muscul Radiol 2016

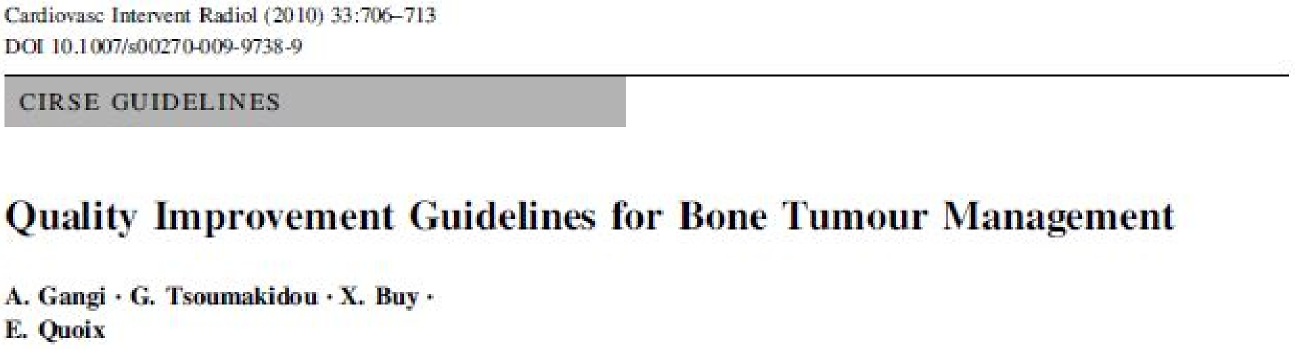
MICROONDE

- Applicazione tramite antenne che generano microonde elettromagnetiche (900MHz-2.45GHz)
- Maggiori temperature di lavoro (150°C)
- Zone di ablazione più ampie in minor tempo
- Minor influenza dell’impedenza tissutale (lesioni osteoblastiche) e dell’»effetto sifone»
- Minor rischio di ustioni cutanee
- Contro: costi maggiori


+
An applied microwave field causes water molecules to rotate billions of times per second, which leads to heat generation.
O+
H-
O+
Electric field polarity
–

Kurup et al., *Ablation of skeletal metastases: current status, J Vasc Interv Radiol 2010*
Kastler et al., *Microwave thermal ablation of spinal metastatic bone tumors, J Vasc Interv Radiol 2014*

….IN QUALI TUMORI?



Cardiovasc Intervent Radiol (2010) 33:706–713
DOI 10.1007/s00270-009-9738-9

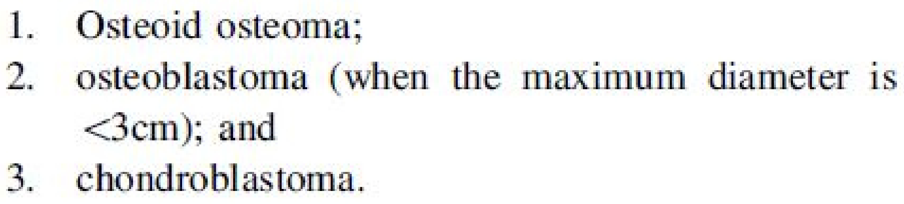
CIRSE GUIDELINES

Quality Improvement Guidelines for Bone Tumour Management

A. Gangi · G. Tsoumakidou · X. Buy ·
E. Quoix

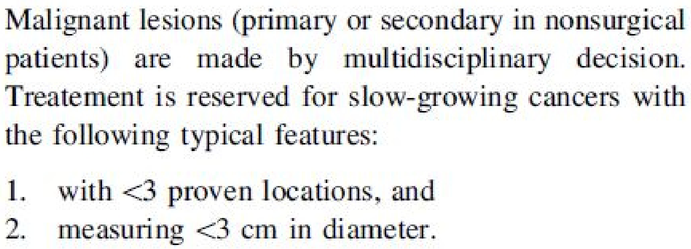
1. INTENTO CURATIVO

LESIONI BENIGNE



1. Osteoid osteoma;
2. osteoblastoma (when the maximum diameter is <3cm); and
3. chondroblastoma.

LESIONI MALIGNE



Malignant lesions (primary or secondary in nonsurgical patients) are made by multidisciplinary decision. Treatement is reserved for slow-growing cancers with the following typical features:

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2. measuring <3 cm in diameter.

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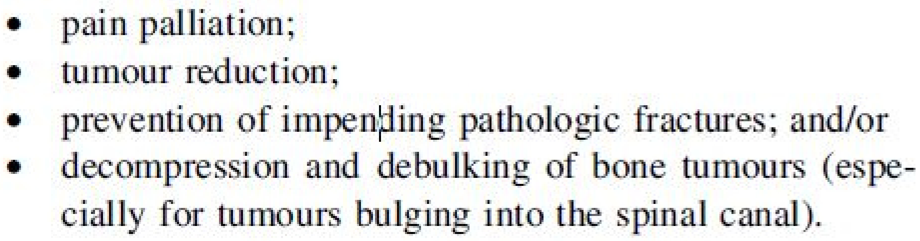
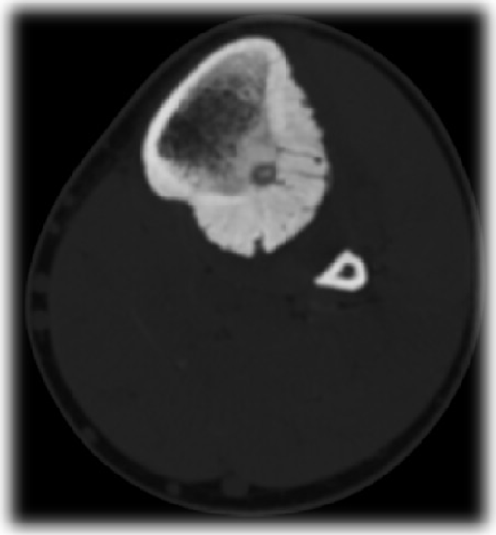
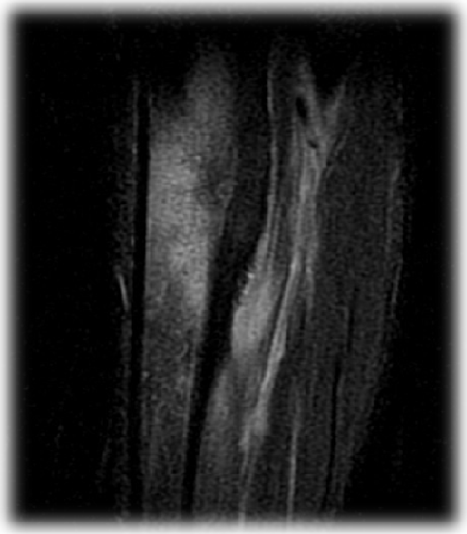


- pain palliation;
- tumour reduction;
- prevention of impending pathologic fractures; and/or
- decompression and debulking of bone tumours (especially for tumours bulging into the spinal canal).

OSTEOMA OSTEOIDE

- 10% dei tumori benigni
- Pazienti giovani (<30 anni), M:F=2-4:1
- Nidus centrale radiotrasparente (tipicamente <15mm) circondato da sclerosi e reazione periostale
- Presentazione clinica tipica (dolore notturno che recede con assunzione di FANS/salicilati)
- La resezione chirurgica è gravata da un tasso di complicanze tra il 35-45%
- Il trattamento percutaneo con ablazione completa del nidus è attualmente considerato il trattamento di scelta data la sua minima invasività, la minore ospedalizzazione, la possibilità di trattare zone ad alto rischio (lesioni intrarticolari, lesioni spinali), i minori costi



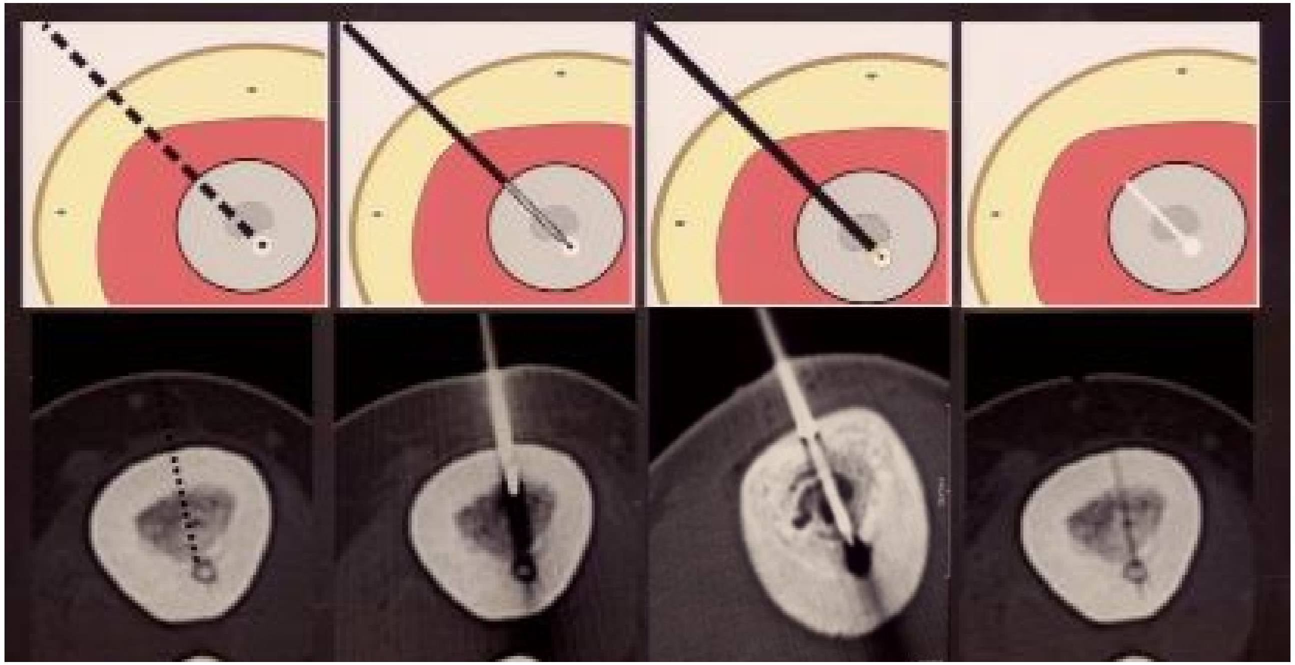


Motamedi et al., *Image-guided treatments of muscuolskeletal tumors, AJR 2016*
Rosenthal et al., *Osteoid osteoma: percutaneous treatment with radiofrequency energy, Radiology 2003*

OSTEOMA OSTEOIDE - PROCEDURA

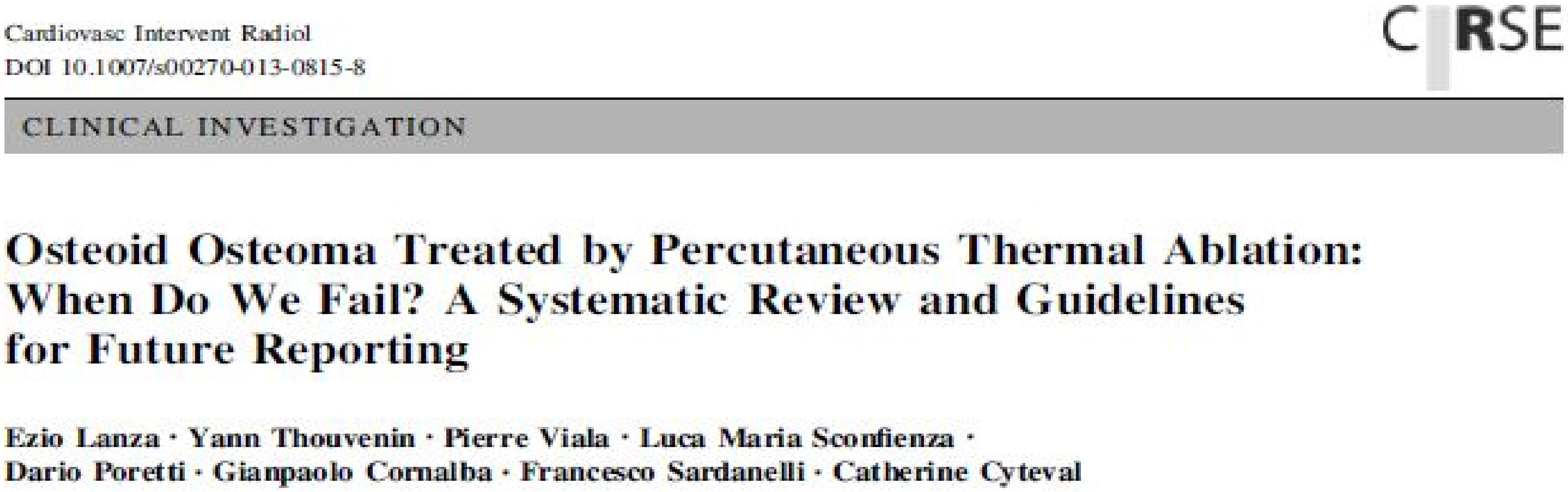
Rosenthal et al., Ablation of osteoid osteomas with a percutaneously placed electrode: a new procedure, Radiology 1992

- Anestesia generale/blocco locoregionale
- **RFA**: 90°C, 5-6 minuti
- **LASER**: singola fibra, 2W (1200J), 6-10 minuti
- Al termine della procedura, 5-10ml di Rupivacaina (2mg/ml) a livello del periostio



Gangi et al, *Guidelines for bone tumor management, Cardiovasc Intervent Radiol 2010*

OSTEOMA OSTEOIDE – RISULTATI



Cardiovasc Intervent Radiol
DOI 10.1007/s00270-013-0815-8

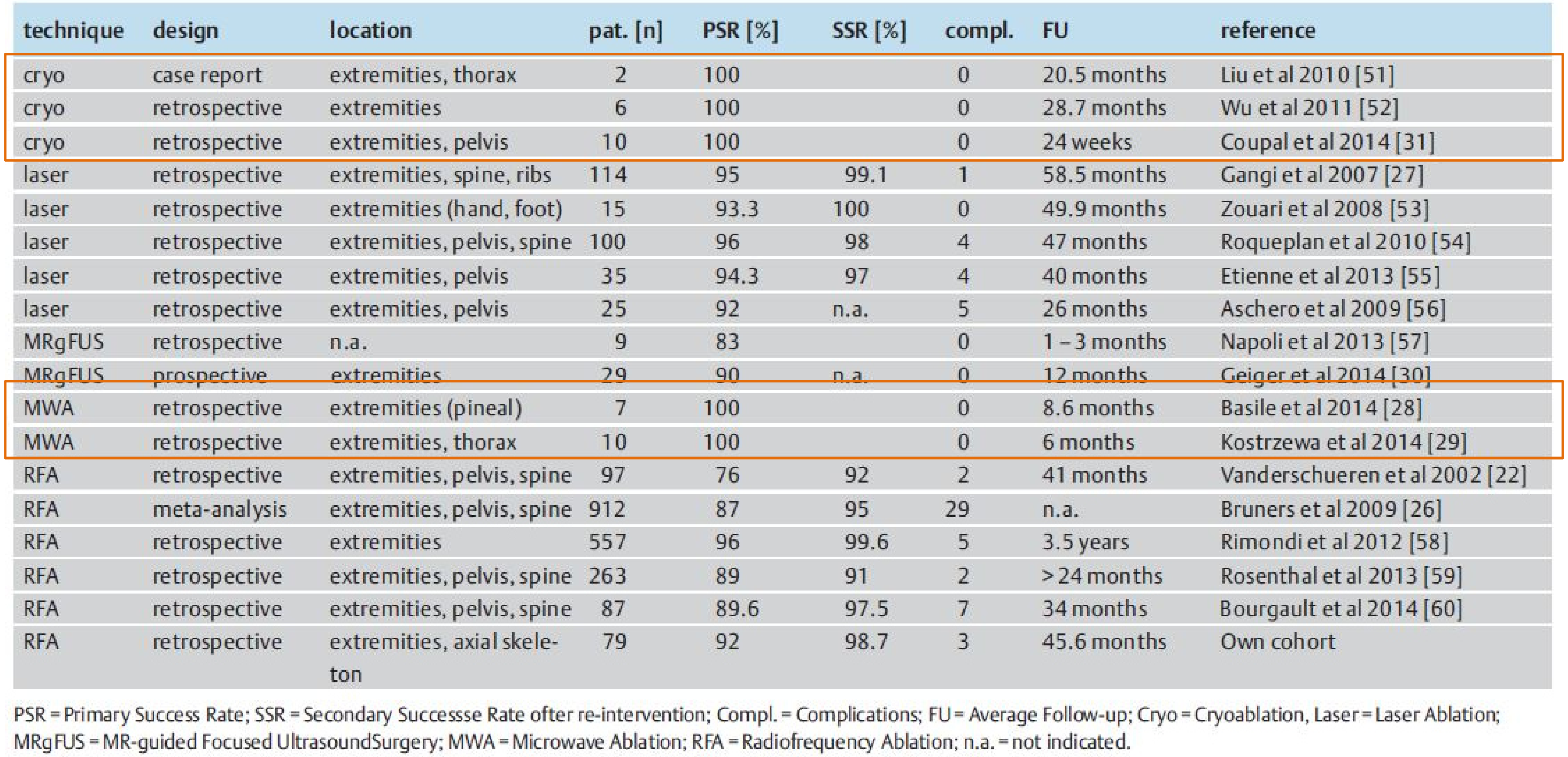
CLINICAL INVESTIGATION

Osteoid Osteoma Treated by Percutaneous Thermal Ablation: When Do We Fail? A Systematic Review and Guidelines for Future Reporting

Ezio Lanza · Yann Thouvenin · Pierre Viala · Luca Maria Sconfienza · Dario Poretti · Gianpaolo Cornalba · Francesco Sardanelli · Catherine Cyteval

- 27 articoli, 1772 pazienti
- 23 **RFA**, 4 **LA**
- Successo tecnico medio: 100%
- Successo clinico (follow-up medio 1 anno): 96%
- Tasso di complicanze: 2.1% (ustioni cutanee, infezioni, lesioni nervose, lesioni device)
- Recidive: 4.9%
- NO DIFFERENZE A SECONDA DELLA LOCALIZZAZIONE DELLA LESIONE E DELLA TECNICA/MATERIALI UTILIZZATI

OSTEOMA OSTEOIDE - RISULTATI



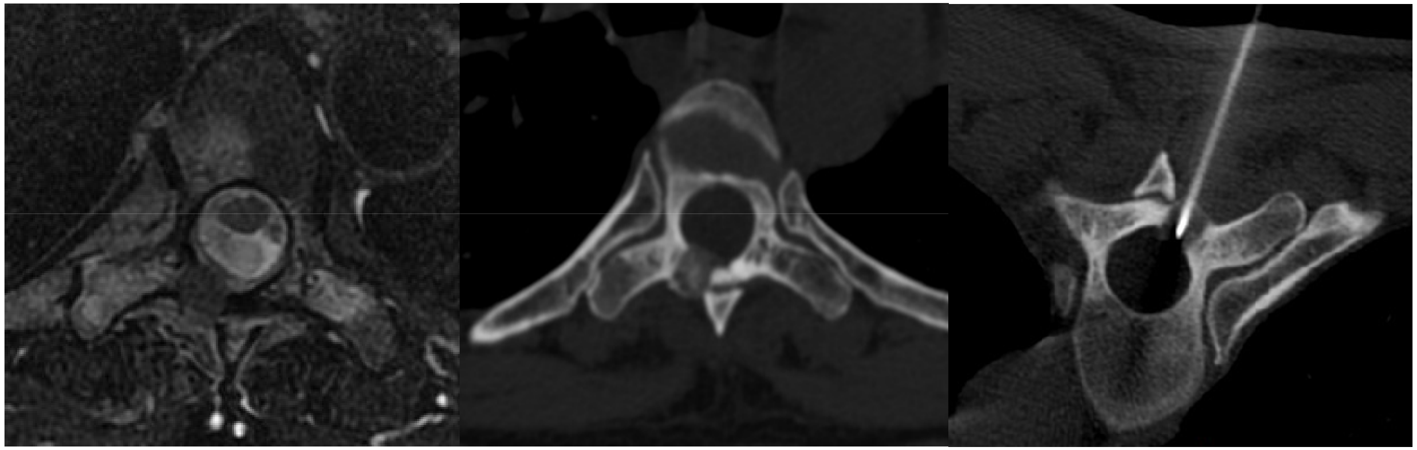
technique	design	location	pat. [n]	PSR [%]	SSR [%]	compl.	FU	reference
cryo	case report	extremities, thorax	2	100		0	20.5 months	Liu et al 2010 [51]
cryo	retrospective	extremities	6	100		0	28.7 months	Wu et al 2011 [52]
cryo	retrospective	extremities, pelvis	10	100		0	24 weeks	Coupal et al 2014 [31]
laser	retrospective	extremities, spine, ribs	114	95	99.1	1	58.5 months	Gangi et al 2007 [27]
laser	retrospective	extremities (hand, foot)	15	93.3	100	0	49.9 months	Zouari et al 2008 [53]
laser	retrospective	extremities, pelvis, spine	100	96	98	4	47 months	Roqueplan et al 2010 [54]
laser	retrospective	extremities, pelvis	35	94.3	97	4	40 months	Etienne et al 2013 [55]
laser	retrospective	extremities, pelvis	25	92	n.a.	5	26 months	Aschero et al 2009 [56]
MRgFUS	retrospective	n.a.	9	83		0	1 – 3 months	Napoli et al 2013 [57]
MRgFUS	prospective	extremities	29	90	n.a.	0	12 months	Geiger et al 2014 [30]
MWA	retrospective	extremities (pineal)	7	100		0	8.6 months	Basile et al 2014 [28]
MWA	retrospective	extremities, thorax	10	100		0	6 months	Kostrzewa et al 2014 [29]
RFA	retrospective	extremities, pelvis, spine	97	76	92	2	41 months	Vanderschueren et al 2002 [22]
RFA	meta-analysis	extremities, pelvis, spine	912	87	95	29	n.a.	Bruners et al 2009 [26]
RFA	retrospective	extremities	557	96	99.6	5	3.5 years	Rimondi et al 2012 [58]
RFA	retrospective	extremities, pelvis, spine	263	89	91	2	> 24 months	Rosenthal et al 2013 [59]
RFA	retrospective	extremities, pelvis, spine	87	89.6	97.5	7	34 months	Bourgault et al 2014 [60]
RFA	retrospective	extremities, axial skeleton	79	92	98.7	3	45.6 months	Own cohort

PSR = Primary Success Rate; SSR = Secondary Successse Rate ofter re-intervention; Compl. = Complications; FU = Average Follow-up; Cryo = Cryoablation, Laser = Laser Ablation; MRgFUS = MR-guided Focused UltrasoundSurgery; MWA = Microwave Ablation; RFA = Radiofrequency Ablation; n.a. = not indicated.

***Ringe et al.**, Thermoablation of bone tumors, Fortschr Rontgenstr 2016*

OSTEOBLASTOMA

- Raro tumore benigno (1% tumori ossei primitivi) istologicamente molto simile all'OO
- Tipicamente lesioni di dimensioni maggiori (>2cm), con minor componente sclerotica
- 40% sono spinali (elementi posteriori)
- Indicazione curativa in lesioni <3cm *(**Gangi et al.,** Guidelines for bone tumor management)*
- Date le maggiori dimensioni e il potenziale coinvolgimento dei tessuti molli, anche la crioablazione può essere utilizzata *(**Tsoumakidou et al.,** Image guided spinal ablation, CVIR 2016)*



Weber et al., Clinical long-term outcome, technical success and cost analysis of radiofrequency ablation for the treatment of osteoblastomas and spinal osteoid osteomas in comparison to open surgical resection, Skeletal Radiol 2015: completa scomparsa del dolore a 30gg 100% vs 50% chirurgia

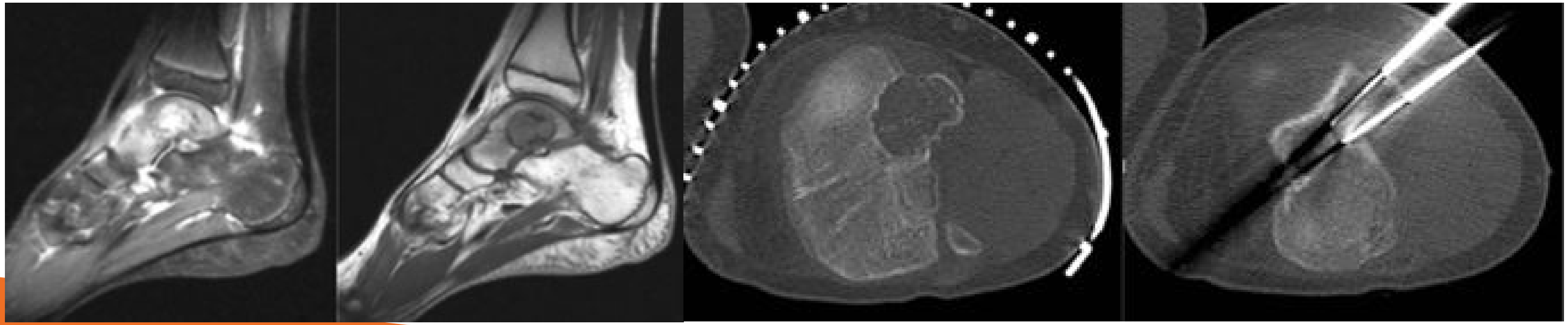
Rehnitz et al., CT guided radiofrequency ablation of osteoid osteoma and osteoblastoma: clinical success and long term follow-up in 77 patients, Eur J Radiol 2012: 81 RFA (65 OO, 12OB), PSR 96.1%, SSR 100%, riduzione significativa VAS (p<.001) in un follow-up a lungo termine (media 38.5 mesi)

CONDROBLASTOMA

- Raro tumore benigno cartilagineo (1% tumori benigni)
- Trattamento tradizionale: curettage chirurgico
- Complicanze chirurgiche frequenti (osteoartrosi precoce, dismetria degli arti) a causa della prossimità alla cartilagine di accrescimento
- Tasso di recidiva 5-40%

Rybak et al., Chondroblastoma: radiofrequency ablation – alternative to surgical resection in selected cases, Radiology 2009: 17 pazienti, riduzione del dolore iniziale del 100%, 6% di recidive (follow-up 41 mesi), inferiore alla media del trattamento chirurgico riportata in letteratura (10-35%)

Xie et al., Radiofrequency ablation of chondroblastoma: long-term clinical and imaging outcomes, Eur Rad 2014: 25 pazienti, follow-up 3 anni, risoluzione completa dei sintomi nell'88%, recidiva in 3 paz (12%) a 16, 22 e 24 mesi



…ALTRE INDICAZIONI

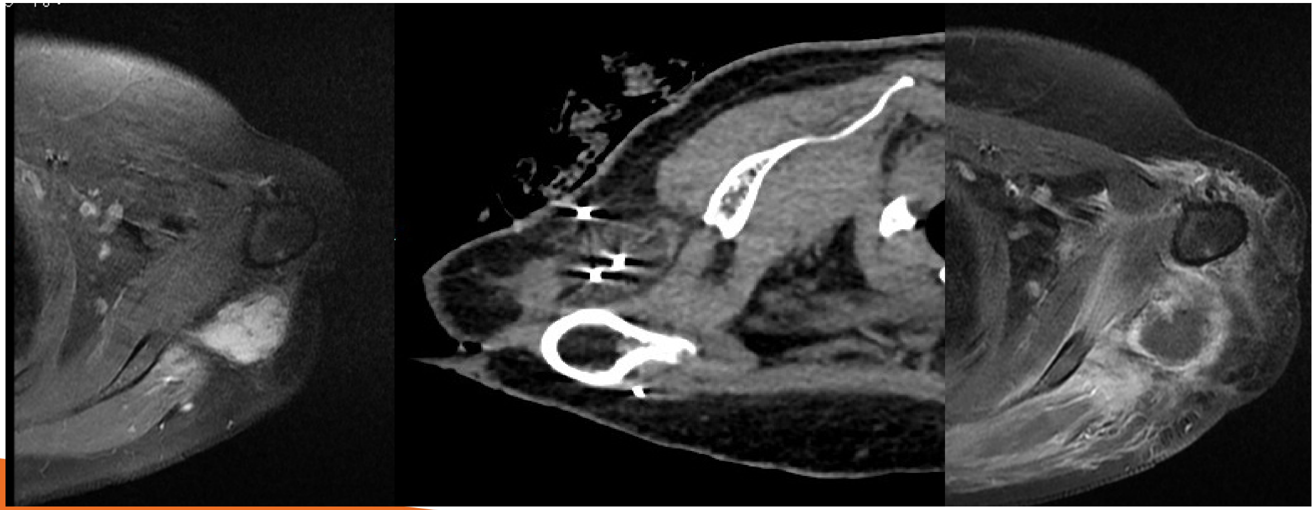
- L'evidenza riguardo la termoablazione di altri tumori è limitata e si basa prevalentemente su case reports o piccole serie di casi.
- Secondo alcune review dello stato dell'arte « essentially any small well defined lesion at imaging can be treated with RF ablation»

(***Rosenthal et al.,*** *Critical review and state of the art in interventional oncology: benign and metastatic disease involving bone, Radiology 2012,* ***Filippiadis et al.,*** *Percutaneous bone lesions ablation, Radiol Med 2014)*

Corby et al, Radiofrequency ablation of solitary eosinophilic granuloma of bone, AJR 2008

Tsoumakidou et al., Treatment of spinal aneurysmal bone cyst using combined image-guided cryoablation and cementoplasty, Skeletal Radiol 2015

Schmitz et al., Percutaneous cryoablation of extraabdominal desmoid tumors: a 10-year experience, AJR 2016: 23 lesioni, follow-up 16 mesi, CR 39.1%, PR 34.8%, PD 1%, no complicanze maggiori



METASTASI OSSEE

Più del 60% dei pazienti con cancro (mammella, prostata, rene, polmone, tiroide) sviluppa metastasi ossee

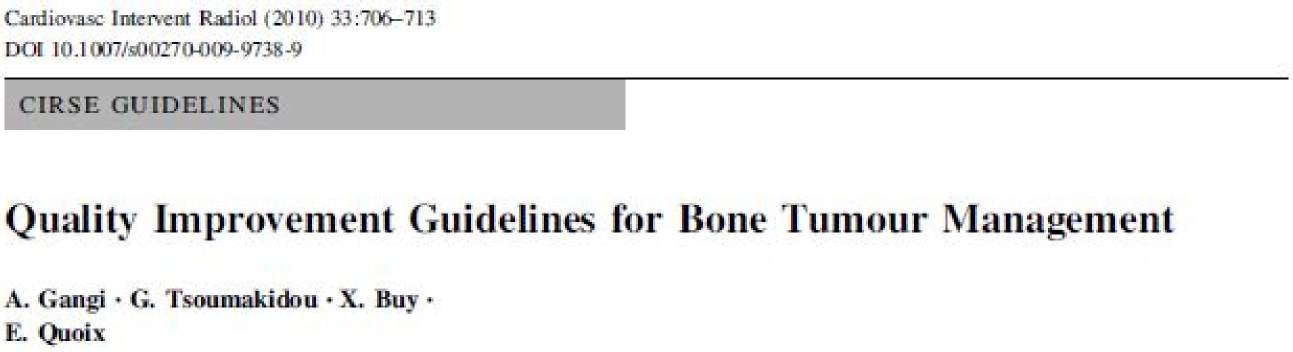
Il dolore osseo metastatico può essere una manifestazione precoce specialmente nelle lesioni litiche, con aumentato rischio di *Eventi Scheletrici Avversi*

I trattamenti convenzionali per il management delle metastasi ossee dolorose includono **terapie sistemiche** (analgesici, *bifosfonati, denosumab*, radiofarmaci) e **trattamenti localizzati** (chirurgia, *radioterapia*)

- Il tasso di risposta alla radioterapia va dal 60 all'80%, con una risposta completa nel 25-30% dei casi ad 1 mese
- L'effetto palliativo compare generalmente entro 4-6 settimane dal trattamento
- Più della metà dei pazienti presenta dolore ricorrente (tempo medio di ricorrenza 2.4 mesi), con il 50% di palliazione in caso di ritrattamento
- Molti pazienti non sono eligibili di trattamento in zone precedentemente irradiate per limiti di tolleranza tissutale

(***Chow et al.***, *Update on the systematic review of palliative radiotherapy trials for bone metastases, Clin Oncol 2012)*

….IN QUALI TUMORI?



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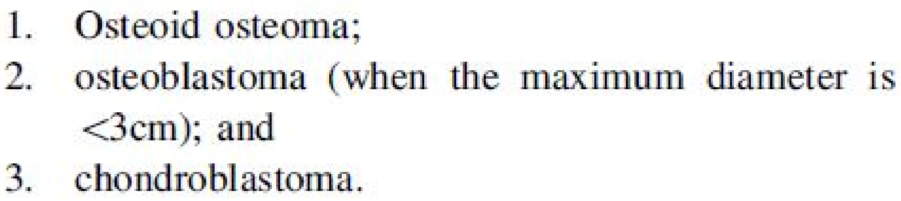

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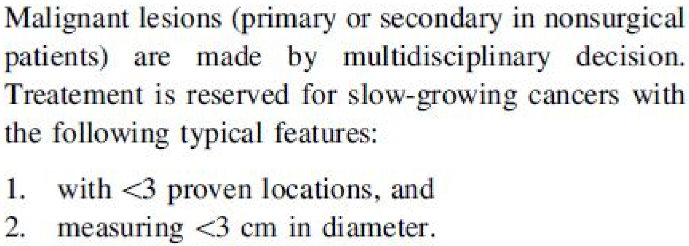

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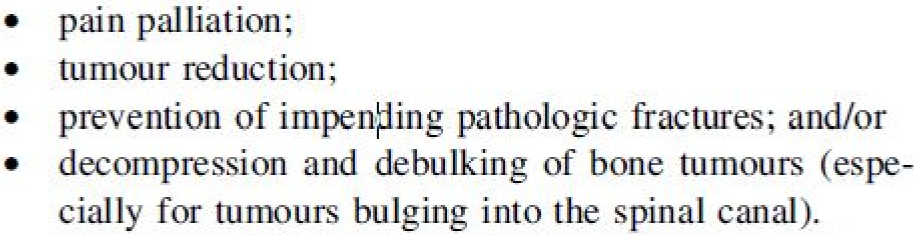

- pain palliation;
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- decompression and debulking of bone tumours (especially for tumours bulging into the spinal canal).

TRATTAMENTI ABLATIVI - SELEZIONE DEI PAZIENTI

- Lesioni osteolitiche o miste, metastasi dei tessuti molli
- Dolore moderato (almeno **>4/10 VAS** in un periodo di 24 ore)
- Correlato a **1 o 2 siti metastatici** evidenti all'imaging
- Controindicazioni assolute: coagulopatie, infezioni cutanee, immunosoppressione

AH MR JOHNSON! ...I DIDN'T RECOGNISE YOU WITH YOUR SKIN ON!
X-R

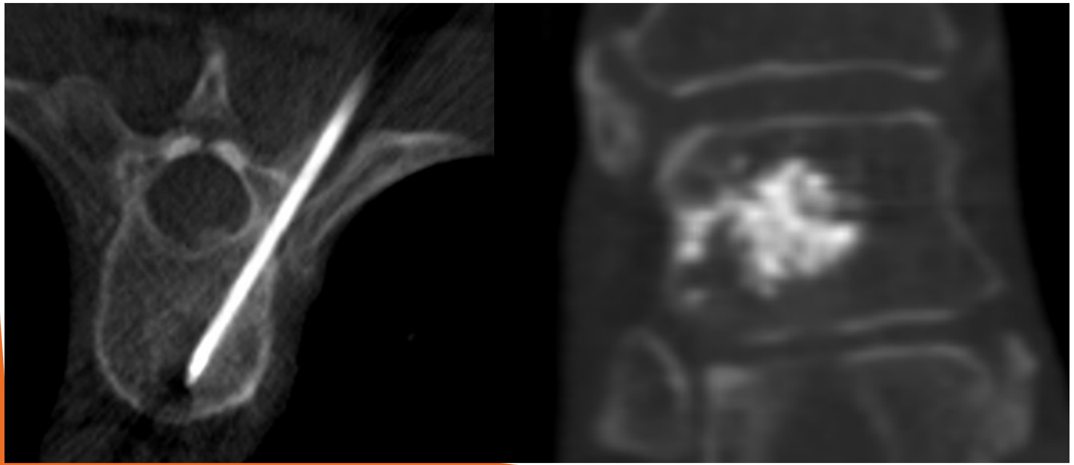
Careers - Become a Radiologist ...

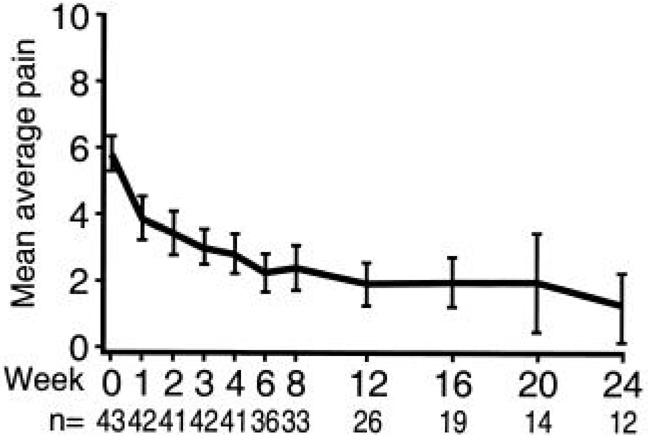
Ringe at al., *Thermoablation of bone tumors, Fortschr Rontgenstr 2015*
Filippiadis et al., *Percutaneous image-guided ablation of bone and soft tissue tumors: a review of available techniques and protective measures, Insights Imaging 2014*
Kurup et al., *Image-guided ablation of bone tumor and soft tissue tumors, Sem Interv Radiol 2010*

METASTASI OSSEE – RFA

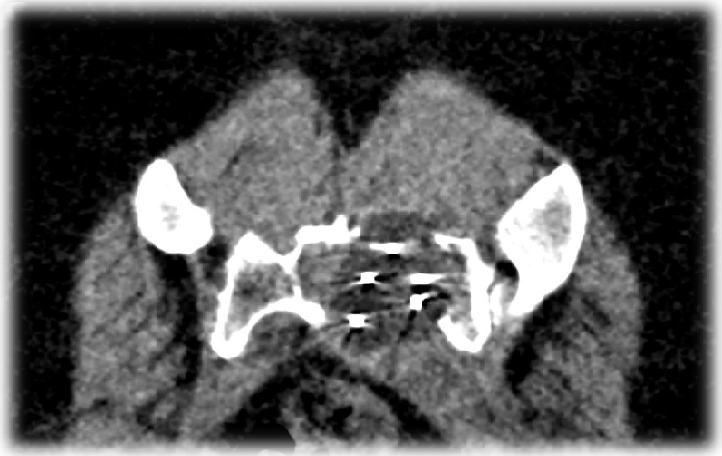
Goetz et al., Percutaneous image-guided radiofrequency ablation of painful metastases involving bone: a multi-center study, J Clin Oncol 2004: 43 pazienti, miglioramento dell'82% dopo il trattamento nel 95% dei pazienti (BPI: 5.8 a 1 settimana, 4.5 a 4 settimane, 3 a 8 settimane e 1.4 a 24 settimane vs 7.9 baseline). 3 complicanze (frattura, incontinenza vescicale transitoria, ustione cutanea)

Dupuy et al., Percutaneous radiofrequency ablation in painful osseous metastases: a multicenter American College of Radiology Imaging Network trial, Cancer 2010: 55 lesioni, dimensione media 5.2 cm, localizzazioni: pelvi, parete toracica, rachide, continuo miglioramento del dolore a 1 mese (<0.001) e a 3 mesi (<0.02), complicanze <10%




Mean average pain
0
2
4
6
8
10
Week 0 1 2 3 4 6 8 12 16 20 24
n= 43 42 41 42 41 36 33 26 19 14 12

METASTASI OSSEE – CRIO

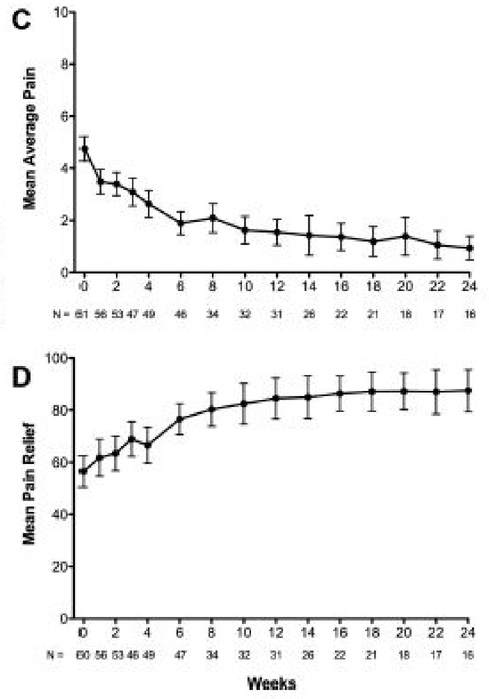


Callstrom et al., Percutaneous image-guided cryoablation of painful metastases involving bone, Cancer 2012: miglioramento del dolore del 75-90% in 46 su 61 pazienti

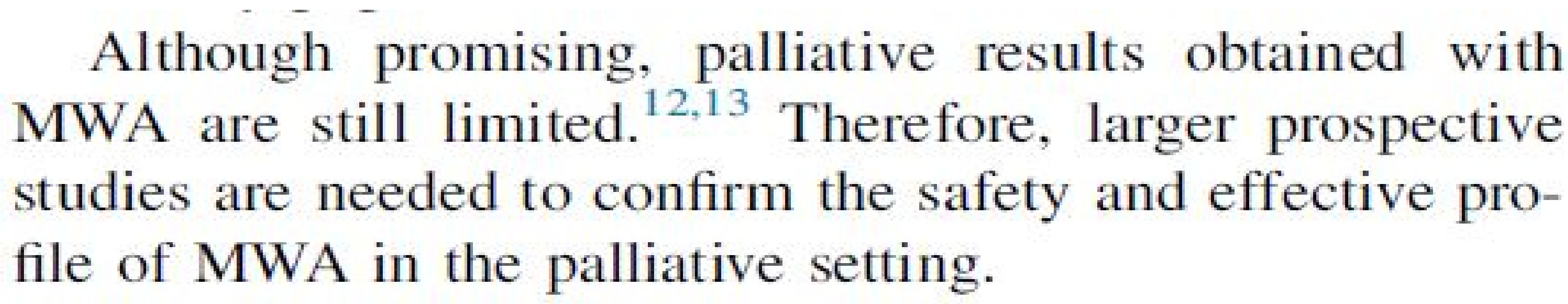
Thacker et al., Palliation of painful metastatic disease involving bone with imaging-guided treatment: comparison of patients' immediate response to radiofrequency ablation and cryoablation, AJR 2011: 58 pazienti (36 crio, 22 RFA), maggiore riduzione dei valori VAS (6.5-3 vs 6-5) a 24h nei pazienti trattati con crioablazione, no differenze nell'outcome a lungo termine

Callstrom et al., Percutaneous image-guided cryoablation of painful metastases involving bone: multicenter trial, Cancer 2013

- 69 lesioni in 61 pazienti
- Dimensioni: 1-11cm
- Riduzione del punteggio BPI medio da 7.1/10 (pre) a 5.1 (*1 settimana*), 4 (1 mese) e 1.4 (24 settimane)
- Riduzione dell'uso di analgesici nell'83% dei pazienti
- Complicanze: 1 caso di osteomielite (2%)

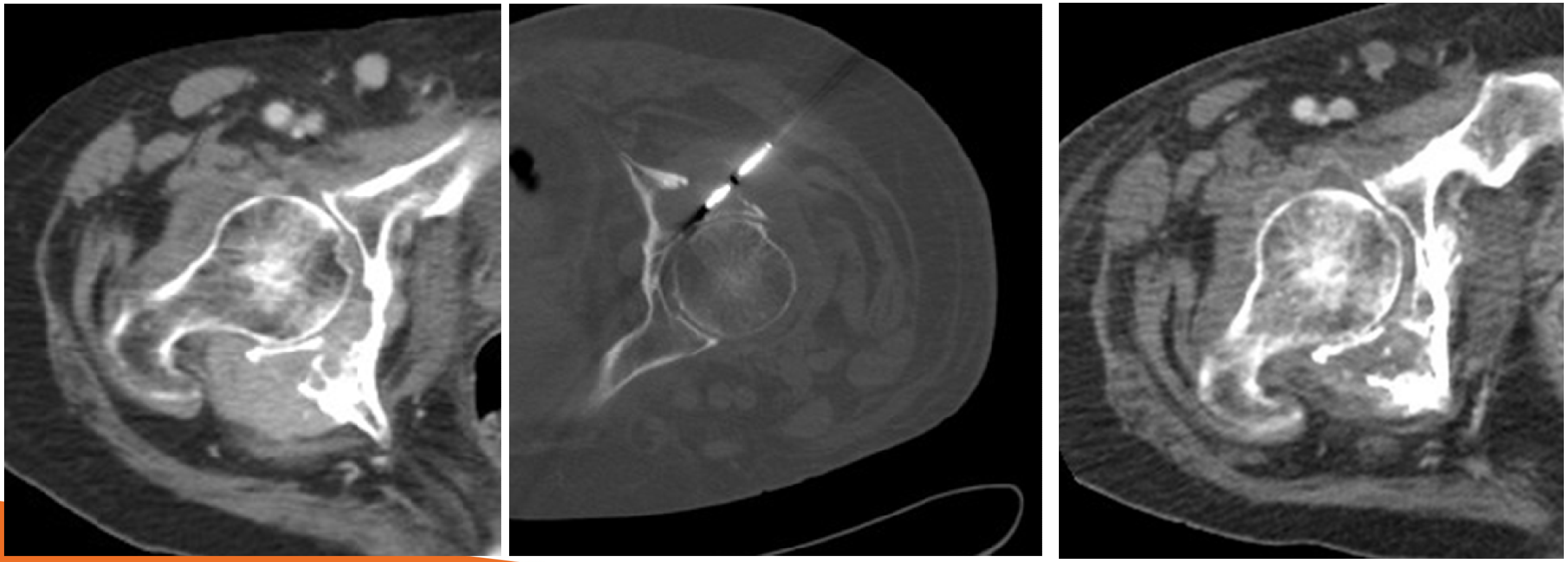


METASTI OSSEE - MW

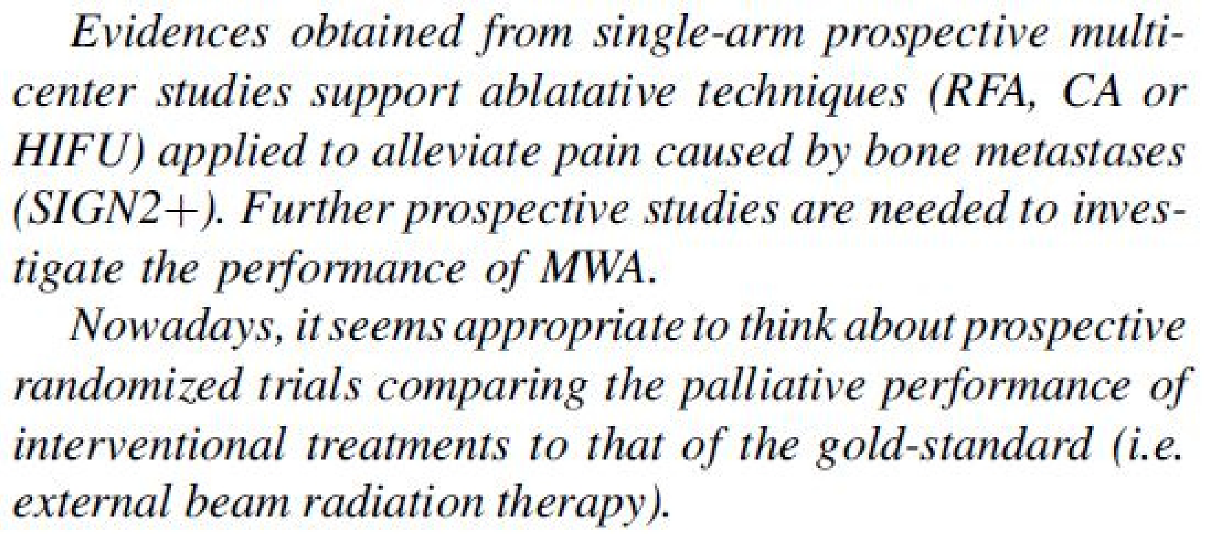


Although promising, palliative results obtained with MWA are still limited.[12,13] Therefore, larger prospective studies are needed to confirm the safety and effective profile of MWA in the palliative setting.

Cazzato et al., *Interventional Radiologist's perspective on the management of bone metastatic disease, EJSO 2015*

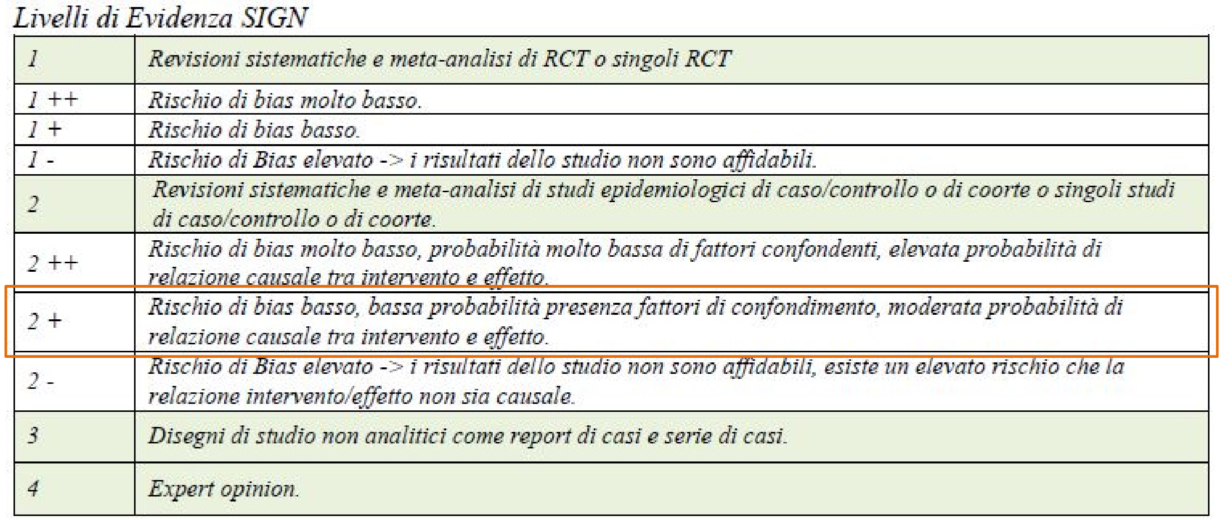


The dark side of the guidelines



Evidences obtained from single-arm prospective multi-center studies support ablatative techniques (RFA, CA or HIFU) applied to alleviate pain caused by bone metastases (SIGN2+). Further prospective studies are needed to investigate the performance of MWA.

Nowadays, it seems appropriate to think about prospective randomized trials comparing the palliative performance of interventional treatments to that of the gold-standard (i.e. external beam radiation therapy).



Livelli di Evidenza SIGN

1	*Revisioni sistematiche e meta-analisi di RCT o singoli RCT*
1 ++	*Rischio di bias molto basso.*
1 +	*Rischio di bias basso.*
1 -	*Rischio di Bias elevato -> i risultati dello studio non sono affidabili.*
2	*Revisioni sistematiche e meta-analisi di studi epidemiologici di caso/controllo o di coorte o singoli studi di caso/controllo o di coorte.*
2 ++	*Rischio di bias molto basso, probabilità molto bassa di fattori confondenti, elevata probabilità di relazione causale tra intervento e effetto.*
2 +	*Rischio di bias basso, bassa probabilità presenza fattori di confondimento, moderata probabilità di relazione causale tra intervento e effetto.*
2 -	*Rischio di Bias elevato -> i risultati dello studio non sono affidabili, esiste un elevato rischio che la relazione intervento/effetto non sia causale.*
3	*Disegni di studio non analitici come report di casi e serie di casi.*
4	*Expert opinion.*

***Cazzato et al.,** Interventional Radiologist's perspective on the management of bone metastatic disease, EJSO 2015*

Di Staso, Zugaro, Masciocchi et al., *A feasibility study of percutaneous radiofrequency ablation followed by radiotherapy in the management of painful osteolytic bone metastases. European Radiology 2011*

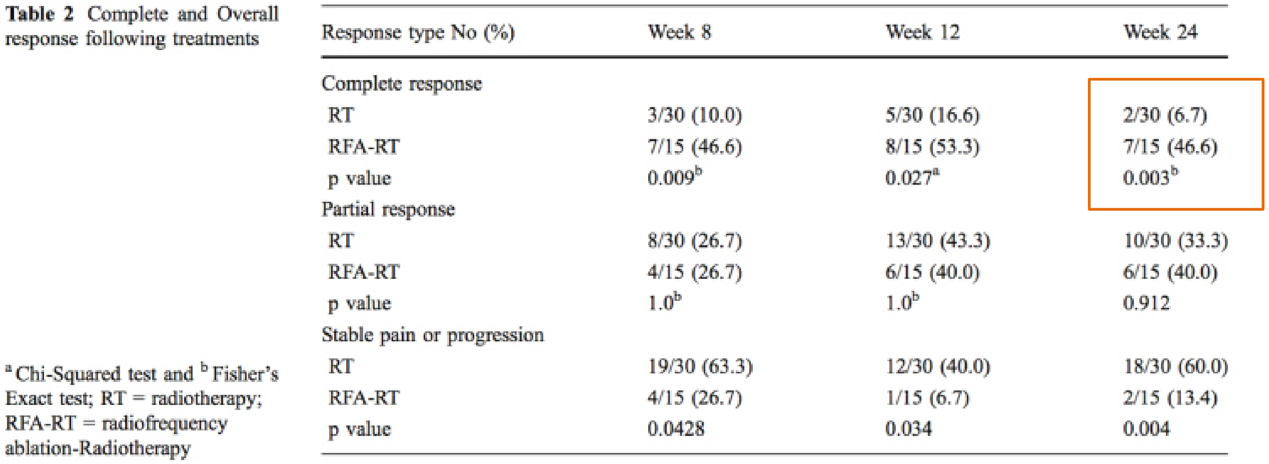


Table 2 Complete and Overall response following treatments

Response type No (%)	Week 8	Week 12	Week 24
Complete response			
RT	3/30 (10.0)	5/30 (16.6)	2/30 (6.7)
RFA-RT	7/15 (46.6)	8/15 (53.3)	7/15 (46.6)
p value	0.009[b]	0.027[a]	0.003[b]
Partial response			
RT	8/30 (26.7)	13/30 (43.3)	10/30 (33.3)
RFA-RT	4/15 (26.7)	6/15 (40.0)	6/15 (40.0)
p value	1.0[b]	1.0[b]	0.912
Stable pain or progression			
RT	19/30 (63.3)	12/30 (40.0)	18/30 (60.0)
RFA-RT	4/15 (26.7)	1/15 (6.7)	2/15 (13.4)
p value	0.0428	0.034	0.004

[a] Chi-Squared test and [b] Fisher's Exact test; RT = radiotherapy; RFA-RT = radiofrequency ablation-Radiotherapy

Di Staso, Zugaro, Masciocchi et al, *Treatment of solitary painful osseous metastases with radiotherapy, cryoablation or combined therapy: propensity matching analysis in 175 patients. PLoS ONE 2015*

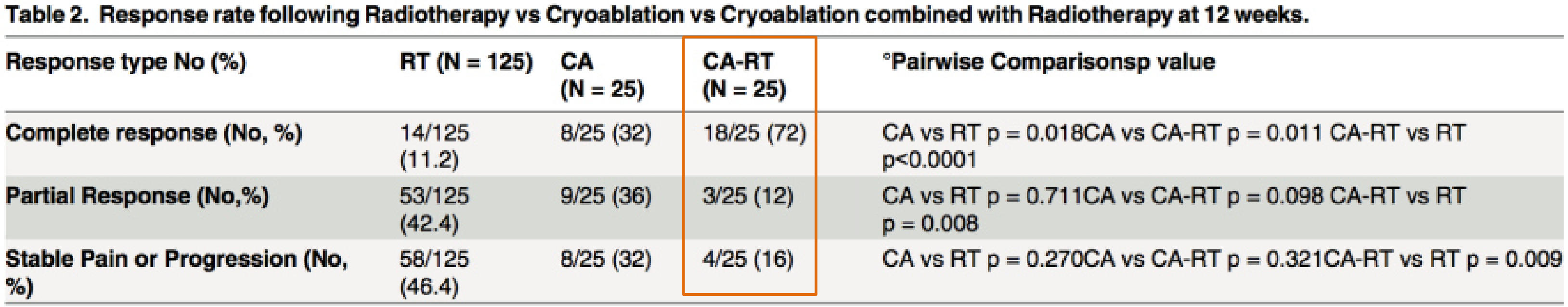
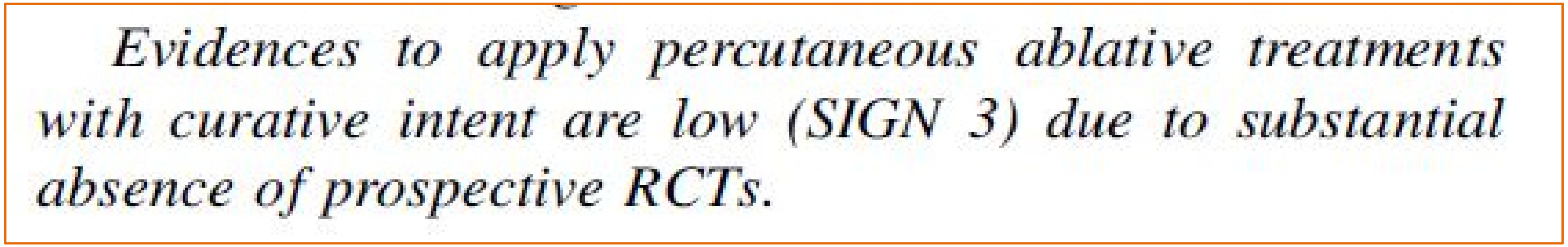


Table 2. Response rate following Radiotherapy vs Cryoablation vs Cryoablation combined with Radiotherapy at 12 weeks.

Response type No (%)	RT (N = 125)	CA (N = 25)	CA-RT (N = 25)	°Pairwise Comparisonsp value
Complete response (No, %)	14/125 (11.2)	8/25 (32)	18/25 (72)	CA vs RT p = 0.018CA vs CA-RT p = 0.011 CA-RT vs RT p<0.0001
Partial Response (No,%)	53/125 (42.4)	9/25 (36)	3/25 (12)	CA vs RT p = 0.711CA vs CA-RT p = 0.098 CA-RT vs RT p = 0.008
Stable Pain or Progression (No, %)	58/125 (46.4)	8/25 (32)	4/25 (16)	CA vs RT p = 0.270CA vs CA-RT p = 0.321CA-RT vs RT p = 0.009

METASTASI OSSEE – OLIGOMETASTASI

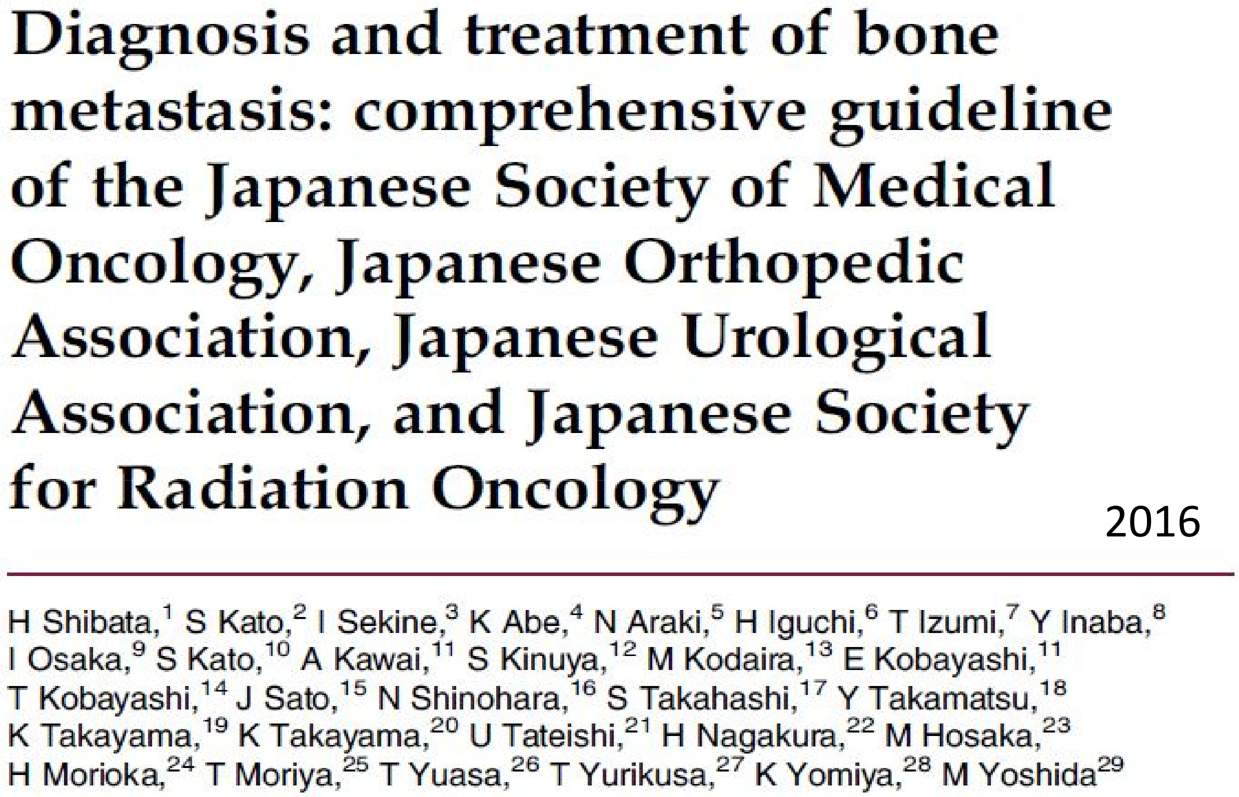
- Nuovo «disease concept»: pazienti con limitato numero di localizzazioni secondarie (<3 - alcuni autori <5 -, <3cm diametro) ***Weichselbaum et al.,*** *Oligometastases revisited, Nat Rev Clin Oncol 2011*
- La resezione chirurgica è il trattamento di scelta quando lo status funzionale del paziente lo permetta
- L'ablazione deve comprendere tutti i margini del tumore (diametro 0.5-1cm maggiore della lesione) ***Cazzato et al.,*** *Interventional radiologist's perspective on the management of bone metastatic disease, EJSO 2015*



Evidences to apply percutaneous ablative treatments with curative intent are low (SIGN 3) due to substantial absence of prospective RCTs.

Deschamps et al., thermal ablation techniques : a curative treatment of bone metastases in selected patients?, Eur Radiol 2014: 122 metastasi trattate con intento curativo in 89 pazienti (74 RFA, 48CA, 38+cementoplastica),follow-up medio 22.8 mesi, risposta completa del 67% ad 1 anno, 3% complicanze maggiori. **Fattori associati con ridotto rischio di fallimento: metastasi metacrone, assenza di erosione corticale, dimensioni <20mm**

METASTASI OSSEE - LINEE GUIDA



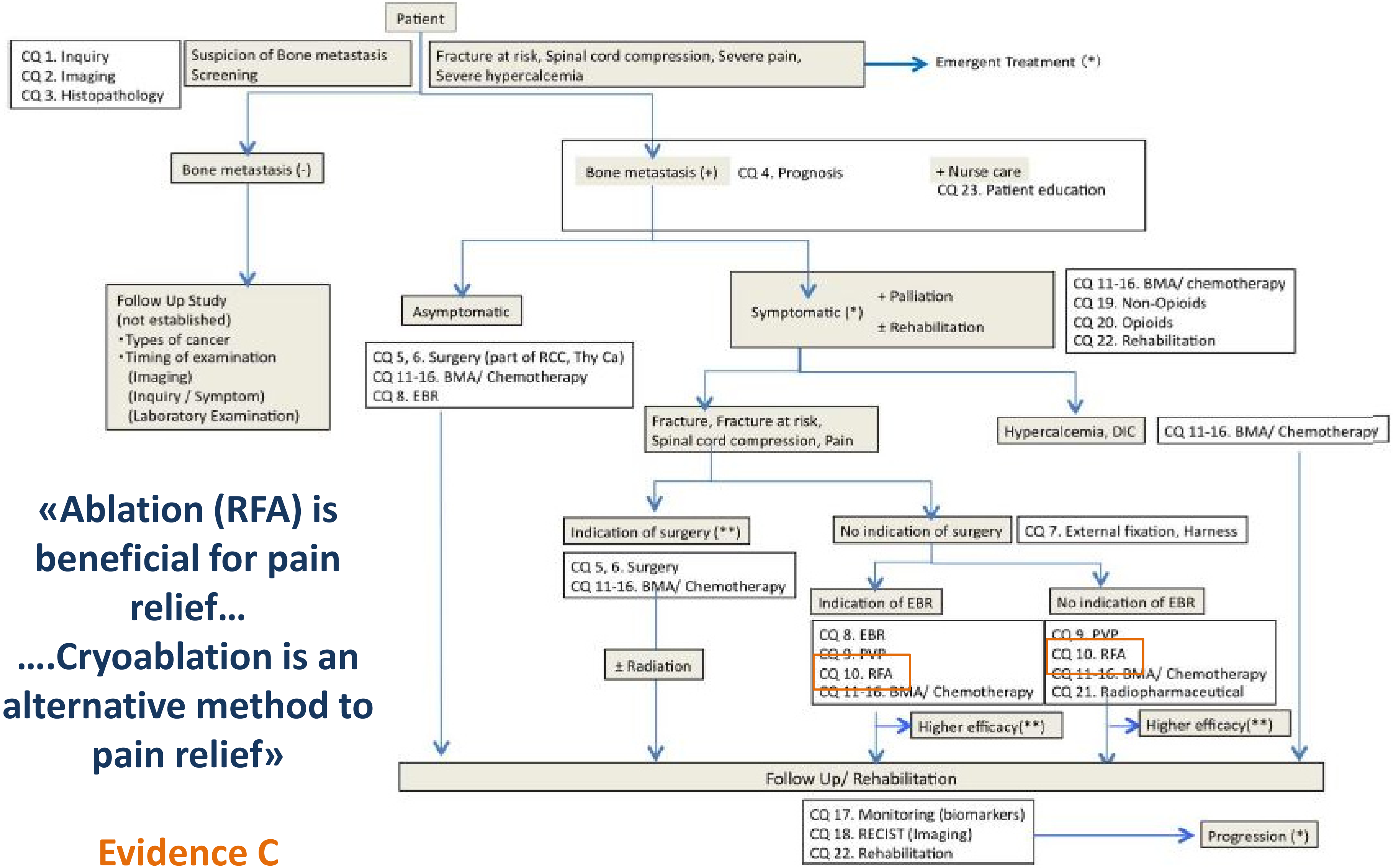
Diagnosis and treatment of bone metastasis: comprehensive guideline of the Japanese Society of Medical Oncology, Japanese Orthopedic Association, Japanese Urological Association, and Japanese Society for Radiation Oncology

2016

H Shibata,[1] S Kato,[2] I Sekine,[3] K Abe,[4] N Araki,[5] H Iguchi,[6] T Izumi,[7] Y Inaba,[8] I Osaka,[9] S Kato,[10] A Kawai,[11] S Kinuya,[12] M Kodaira,[13] E Kobayashi,[11] T Kobayashi,[14] J Sato,[15] N Shinohara,[16] S Takahashi,[17] Y Takamatsu,[18] K Takayama,[19] K Takayama,[20] U Tateishi,[21] H Nagakura,[22] M Hosaka,[23] H Morioka,[24] T Moriya,[25] T Yuasa,[26] T Yurikusa,[27] K Yomiya,[28] M Yoshida[29]

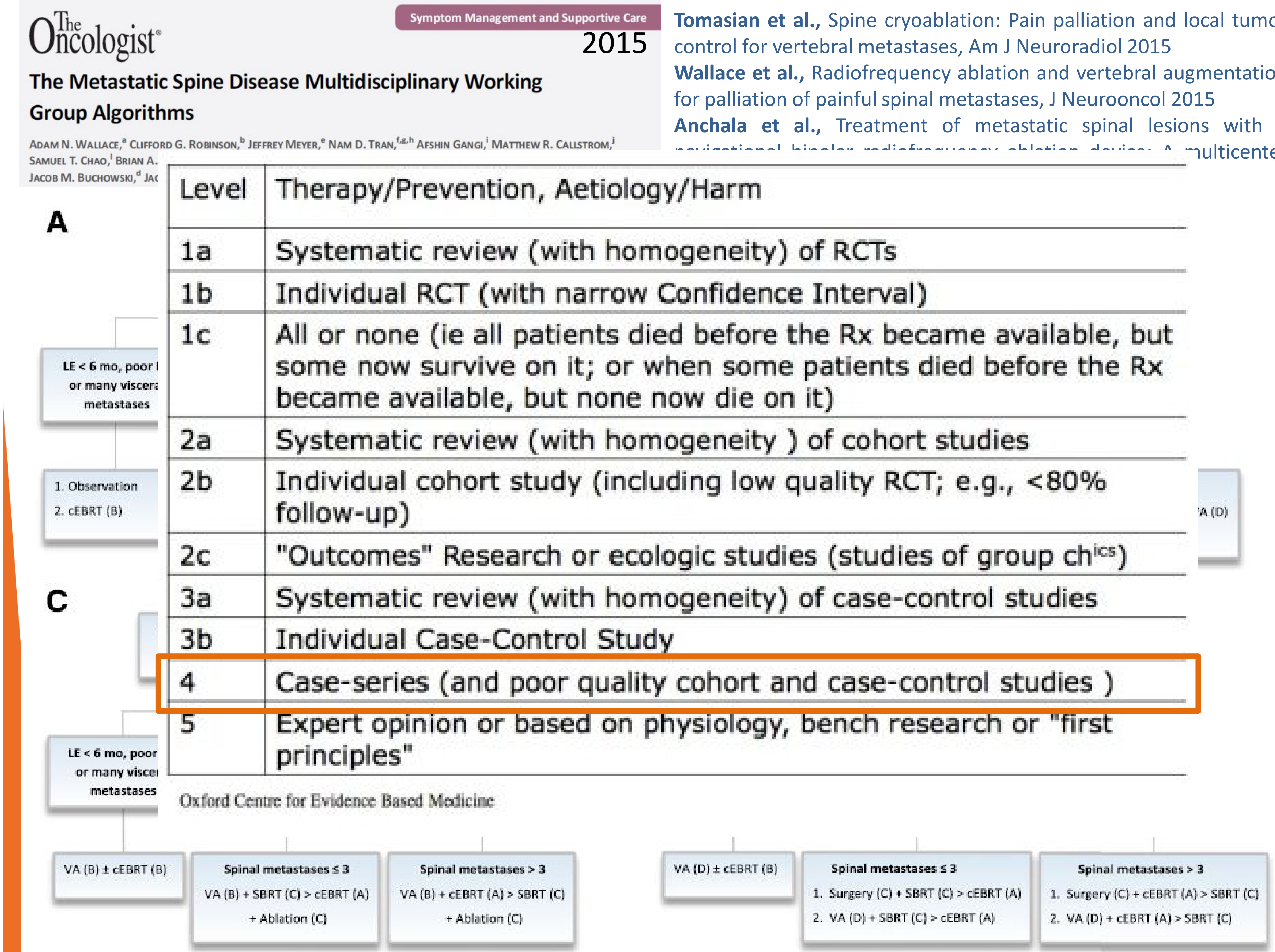
- ***Callstrom et al.,*** *Painful metastases involving bone: percutaneous image-guided cryoablation - prospective trial interim analysis. Radiology 2006*
- ***Goetz et al.****, Percutaneous image-guided radiofrequency ablation of painful metastases involving bone: a multicenter study. J Clin Oncol 2004*

The dark side of the guidelines


Patient
CQ 1. Inquiry
CQ 2. Imaging
CQ 3. Histopathology
Suspicion of Bone metastasis Screening
Fracture at risk, Spinal cord compression, Severe pain, Severe hypercalcemia
Emergent Treatment (*)
Bone metastasis (-)
Bone metastasis (+)
CQ 4. Prognosis
+ Nurse care
CQ 23. Patient education
Follow Up Study (not established)
·Types of cancer
·Timing of examination
(Imaging)
(Inquiry / Symptom)
(Laboratory Examination)
Asymptomatic
CQ 5, 6. Surgery (part of RCC, Thy Ca)
CQ 11-16. BMA/ Chemotherapy
CQ 8. EBR
Symptomatic (*)
+ Palliation
± Rehabilitation
CQ 11-16. BMA/ chemotherapy
CQ 19. Non-Opioids
CQ 20. Opioids
CQ 22. Rehabilitation
Fracture, Fracture at risk, Spinal cord compression, Pain
Hypercalcemia, DIC
CQ 11-16. BMA/ Chemotherapy
Indication of surgery (**)
CQ 5, 6. Surgery
CQ 11-16. BMA/ Chemotherapy
± Radiation
No indication of surgery
CQ 7. External fixation, Harness
Indication of EBR
CQ 8. EBR
~~CQ 9. PVP~~
CQ 10. RFA
~~CQ 11-16. BMA/~~ Chemotherapy
No indication of EBR
~~CQ 9. PVP~~
CQ 10. RFA
~~CQ 11-16. BMA/~~ Chemotherapy
CQ 21. Radiopharmaceutical
Higher efficacy(**)
Higher efficacy(**)
Follow Up/ Rehabilitation
CQ 17. Monitoring (biomarkers)
CQ 18. RECIST (Imaging)
CQ 22. Rehabilitation
Progression (*)

«Ablation (RFA) is beneficial for pain relief…
….Cryoablation is an alternative method to pain relief»

Evidence C



The Oncologist®

Symptom Management and Supportive Care

2015

The Metastatic Spine Disease Multidisciplinary Working Group Algorithms

Adam N. Wallace,[a] Clifford G. Robinson,[b] Jeffrey Meyer,[e] Nam D. Tran,[f,g,h] Afshin Gangi,[i] Matthew R. Callstrom,[j] Samuel T. Chao,[l] Brian A.
Jacob M. Buchowski,[d] Jac

Tomasian et al., Spine cryoablation: Pain palliation and local tumor control for vertebral metastases, Am J Neuroradiol 2015

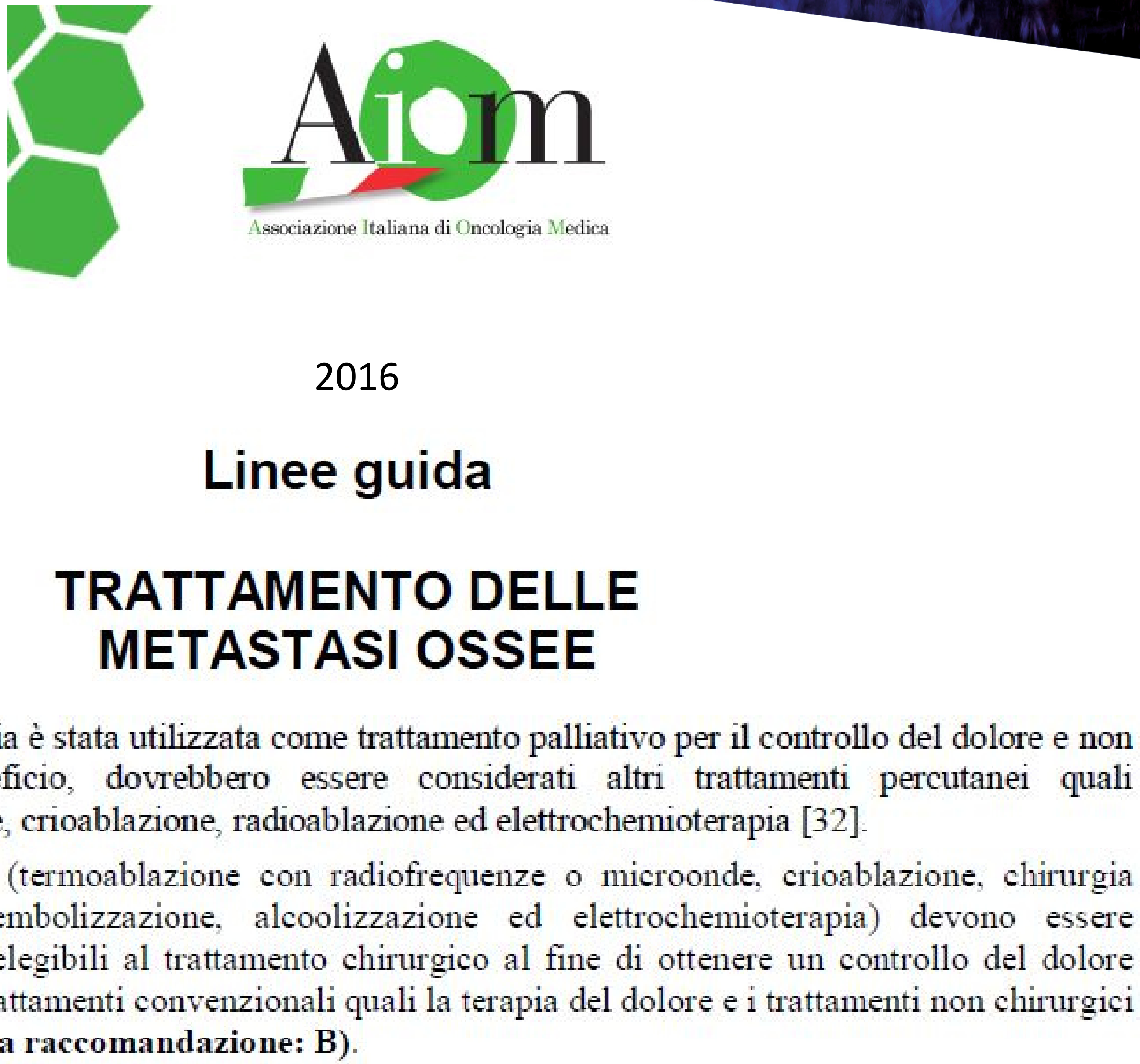
Wallace et al., Radiofrequency ablation and vertebral augmentation for palliation of painful spinal metastases, J Neurooncol 2015

Anchala et al., Treatment of metastatic spinal lesions with a navigational bipolar radiofrequency ablation device: A multicenter

Level	Therapy/Prevention, Aetiology/Harm
1a	Systematic review (with homogeneity) of RCTs
1b	Individual RCT (with narrow Confidence Interval)
1c	All or none (ie all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)
2c	"Outcomes" Research or ecologic studies (studies of group ch^{ics})
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual Case-Control Study
4	Case-series (and poor quality cohort and case-control studies)
5	Expert opinion or based on physiology, bench research or "first principles"

Oxford Centre for Evidence Based Medicine

A
LE < 6 mo, poor
or many viscera
metastases
1. Observation
2. cEBRT (B)
A (D)
C
LE < 6 mo, poor
or many visce
metastases
VA (B) ± cEBRT (B)
Spinal metastases ≤ 3
VA (B) + SBRT (C) > cEBRT (A)
+ Ablation (C)
Spinal metastases > 3
VA (B) + cEBRT (A) > SBRT (C)
+ Ablation (C)
VA (D) ± cEBRT (B)
Spinal metastases ≤ 3
1. Surgery (C) + SBRT (C) > cEBRT (A)
2. VA (D) + SBRT (C) > cEBRT (A)
Spinal metastases > 3
1. Surgery (C) + cEBRT (A) > SBRT (C)
2. VA (D) + cEBRT (A) > SBRT (C)



Associazione Italiana di Oncologia Medica

2016

Linee guida

TRATTAMENTO DELLE METASTASI OSSEE

In pazienti in cui la radioterapia è stata utilizzata come trattamento palliativo per il controllo del dolore e non ha determinato alcun beneficio, dovrebbero essere considerati altri trattamenti percutanei quali alcolizzazione, termoablazione, crioablazione, radioablazione ed elettrochemioterapia [32].

Le terapie mini-invasive [5] (termoablazione con radiofrequenze o microonde, crioablazione, chirurgia focalizzata ad ultrasuoni, embolizzazione, alcoolizzazione ed elettrochemioterapia) devono essere considerate nei pazienti non elegibili al trattamento chirurgico al fine di ottenere un controllo del dolore altrimenti non responsivo ai trattamenti convenzionali quali la terapia del dolore e i trattamenti non chirurgici **(Livello di evidenza: V; Forza raccomandazione: B)**.

The dark side of the guidelines

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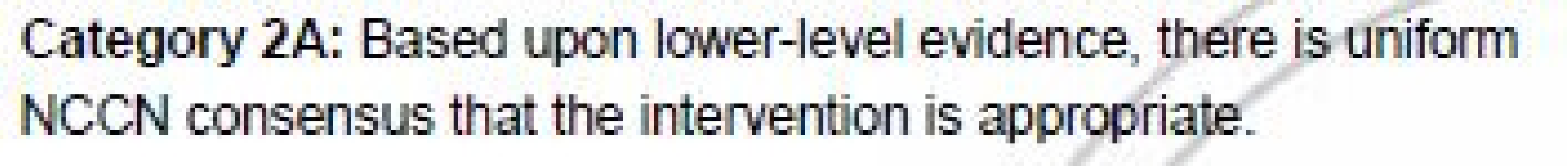
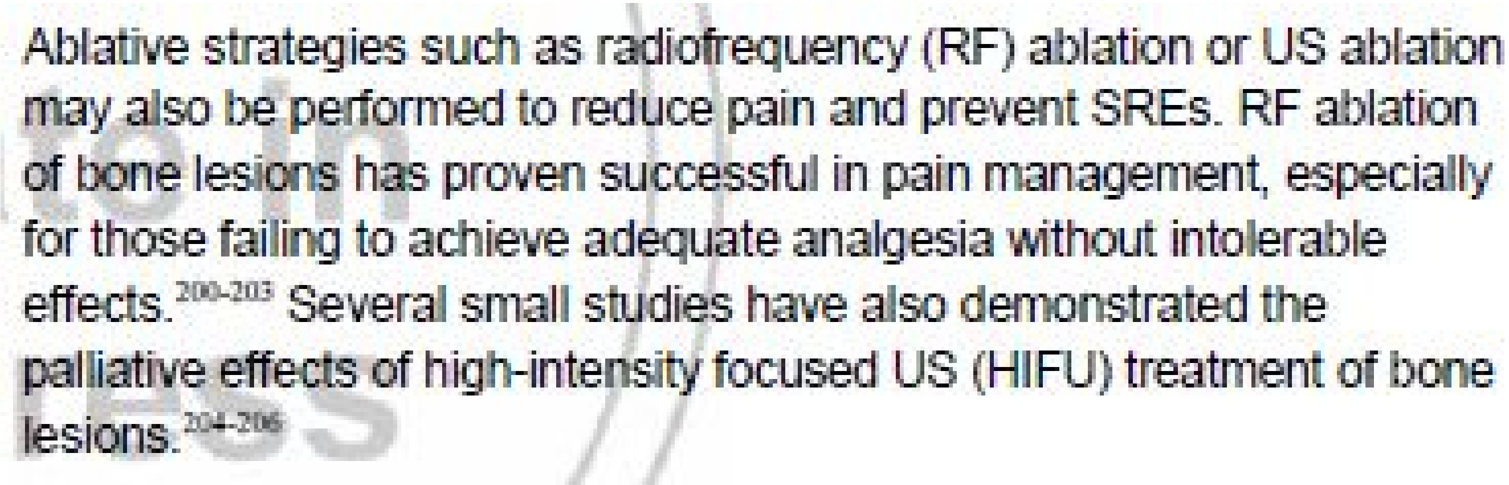


Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Adult Cancer Pain

Version 1.2017 — March 20, 2017



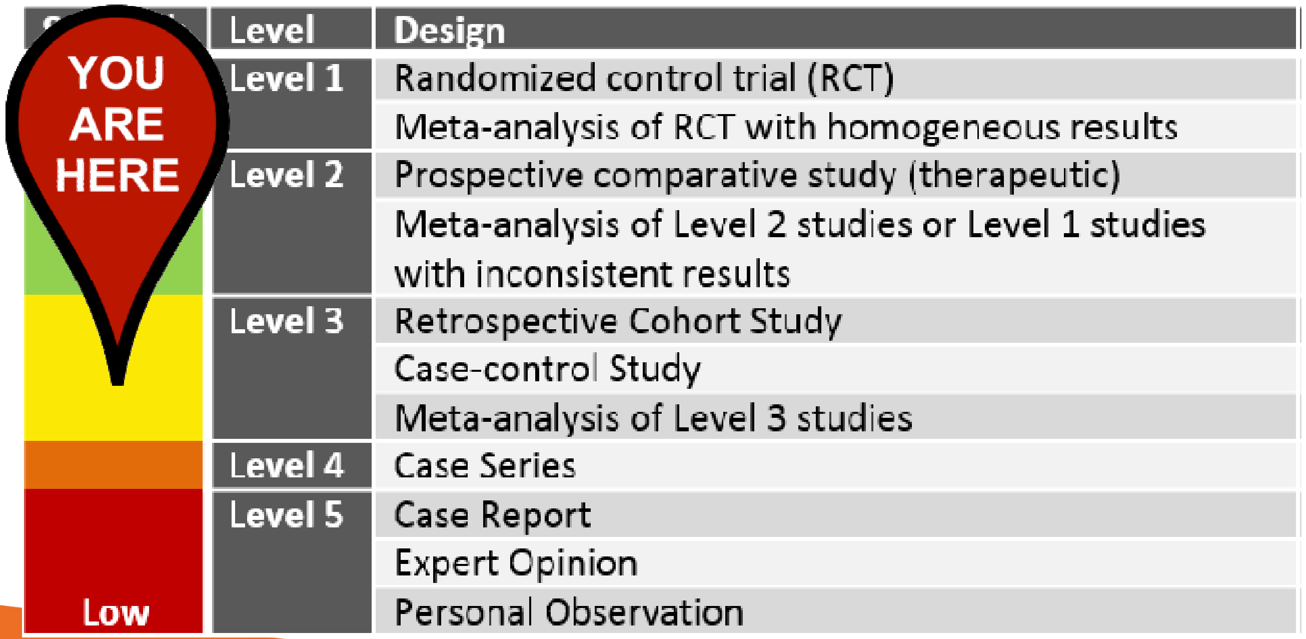
Ablative strategies such as radiofrequency (RF) ablation or US ablation may also be performed to reduce pain and prevent SREs. RF ablation of bone lesions has proven successful in pain management, especially for those failing to achieve adequate analgesia without intolerable effects.[200-203] Several small studies have also demonstrated the palliative effects of high-intensity focused US (HIFU) treatment of bone lesions.[204-206]

Goetz et al., *Percutaneous image-guided radiofrequency ablation of painful metastases involving bone: a multi-center study, J Clin Oncol 2004*

Dupuy et al., *Percutaneous radiofrequency ablation in painful osseous metastases: a multicenter American College of Radiology Imaging Network trial, Cancer 2010*

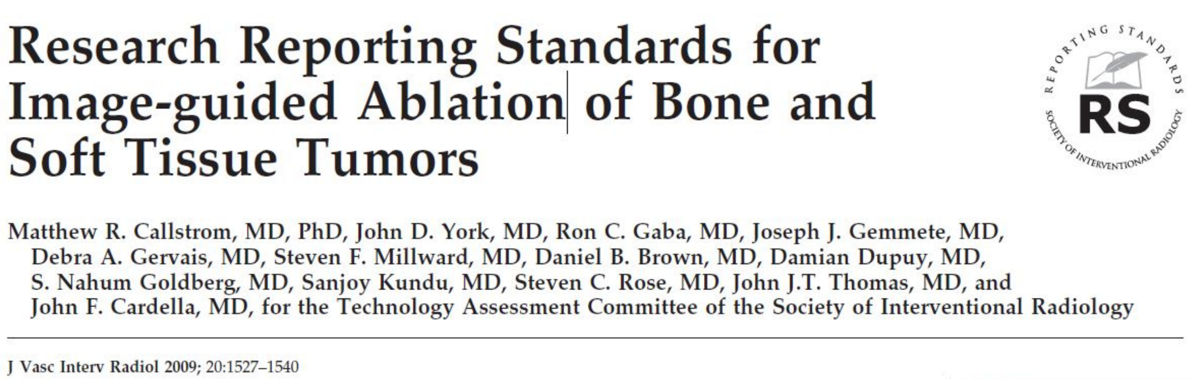
CONCLUSIONI

- I trattamenti ablativi percutanei rappresentano un fiorente campo nella radiologia interventistica MSK
- L'evidenza della letteratura è supportata da studi di livello III o IV, con una grande variabilità nei criteri di selezione, una significativa eterogeneità di demografia dei pazienti, tumori e tecnica, differenti definizioni del successo tecnico e dell'outcome oncologico che spesso ne determinano l'esclusione dalle review sistematiche
- Per ottenere una sempre maggiore accettazione clinica, l'utilizzo di tecniche ablative deve essere supportato da studi prospettici ben strutturati e studi clinici randomizzati in comparazione con altre metodiche di trattamento


YOU
ARE
HERE

	Level	Design
	Level 1	Randomized control trial (RCT)
		Meta-analysis of RCT with homogeneous results
	Level 2	Prospective comparative study (therapeutic)
		Meta-analysis of Level 2 studies or Level 1 studies with inconsistent results
	Level 3	Retrospective Cohort Study
		Case-control Study
		Meta-analysis of Level 3 studies
	Level 4	Case Series
	Level 5	Case Report
		Expert Opinion
Low		Personal Observation

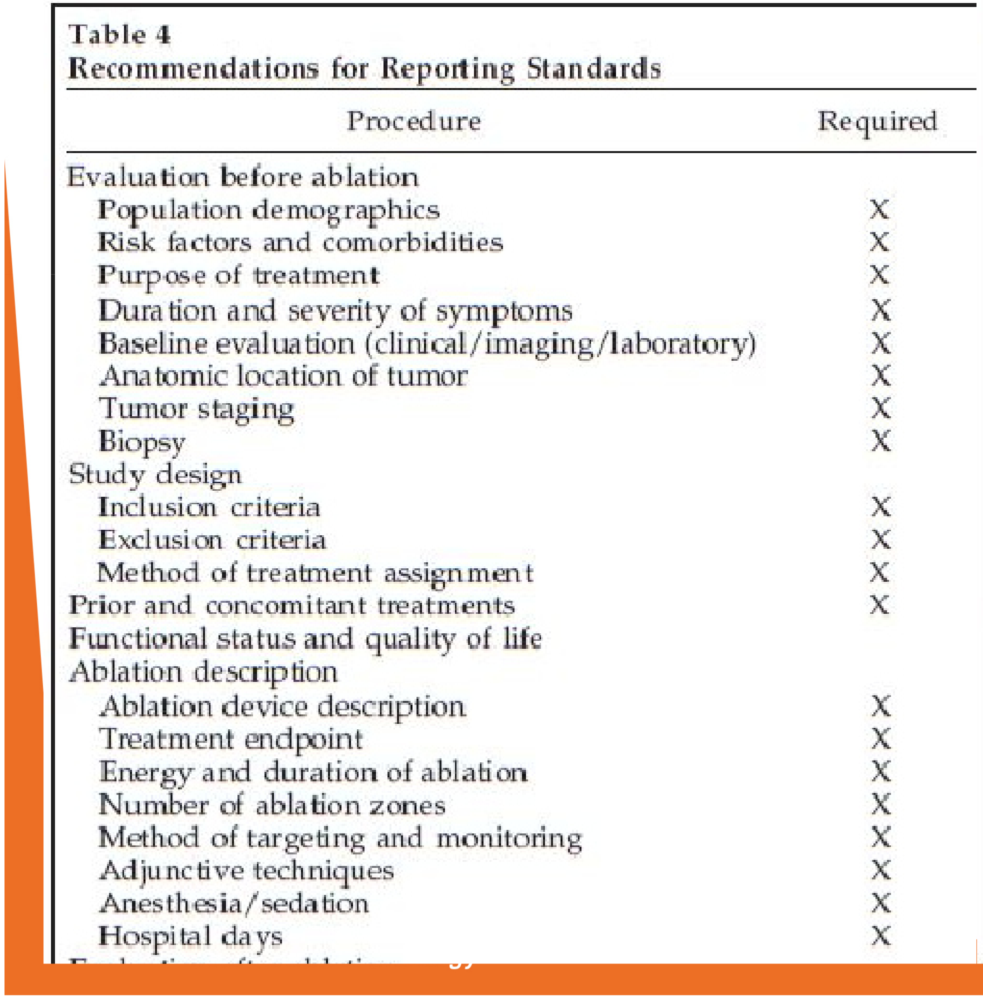
The dark side of the guidelines



Research Reporting Standards for Image-guided Ablation of Bone and Soft Tissue Tumors

Matthew R. Callstrom, MD, PhD, John D. York, MD, Ron C. Gaba, MD, Joseph J. Gemmete, MD,
Debra A. Gervais, MD, Steven F. Millward, MD, Daniel B. Brown, MD, Damian Dupuy, MD,
S. Nahum Goldberg, MD, Sanjoy Kundu, MD, Steven C. Rose, MD, John J.T. Thomas, MD, and
John F. Cardella, MD, for the Technology Assessment Committee of the Society of Interventional Radiology

J Vasc Interv Radiol 2009; 20:1527–1540



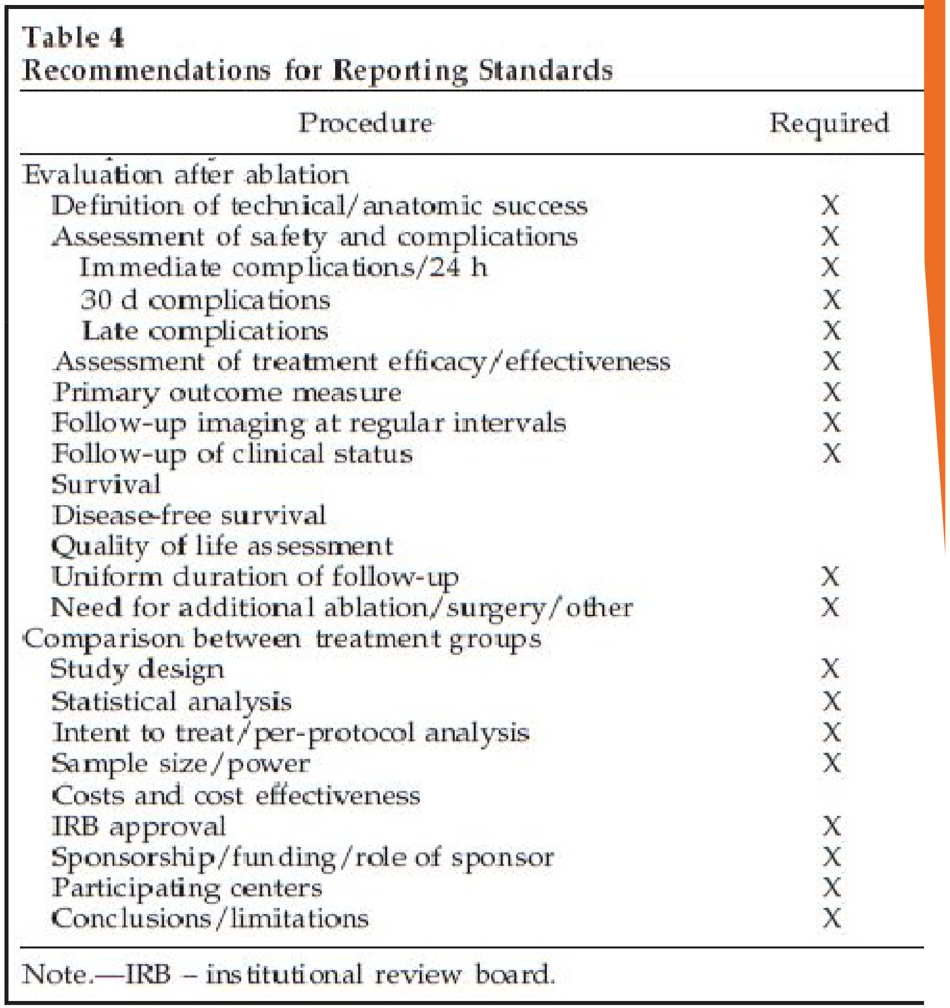


Table 4
Recommendations for Reporting Standards

Procedure	Required
Evaluation before ablation	
Population demographics	X
Risk factors and comorbidities	X
Purpose of treatment	X
Duration and severity of symptoms	X
Baseline evaluation (clinical/imaging/laboratory)	X
Anatomic location of tumor	X
Tumor staging	X
Biopsy	X
Study design	
Inclusion criteria	X
Exclusion criteria	X
Method of treatment assignment	X
Prior and concomitant treatments	X
Functional status and quality of life	
Ablation description	
Ablation device description	X
Treatment endpoint	X
Energy and duration of ablation	X
Number of ablation zones	X
Method of targeting and monitoring	X
Adjunctive techniques	X
Anesthesia/sedation	X
Hospital days	X
Evaluation after ablation	
Definition of technical/anatomic success	X
Assessment of safety and complications	X
Immediate complications/24 h	X
30 d complications	X
Late complications	X
Assessment of treatment efficacy/effectiveness	X
Primary outcome measure	X
Follow-up imaging at regular intervals	X
Follow-up of clinical status	X
Survival	
Disease-free survival	
Quality of life assessment	
Uniform duration of follow-up	X
Need for additional ablation/surgery/other	X
Comparison between treatment groups	
Study design	X
Statistical analysis	X
Intent to treat/per-protocol analysis	X
Sample size/power	X
Costs and cost effectiveness	
IRB approval	X
Sponsorship/funding/role of sponsor	X
Participating centers	X
Conclusions/limitations	X

Note.—IRB – institutional review board.

WE WANT YOU FOR RCTs!