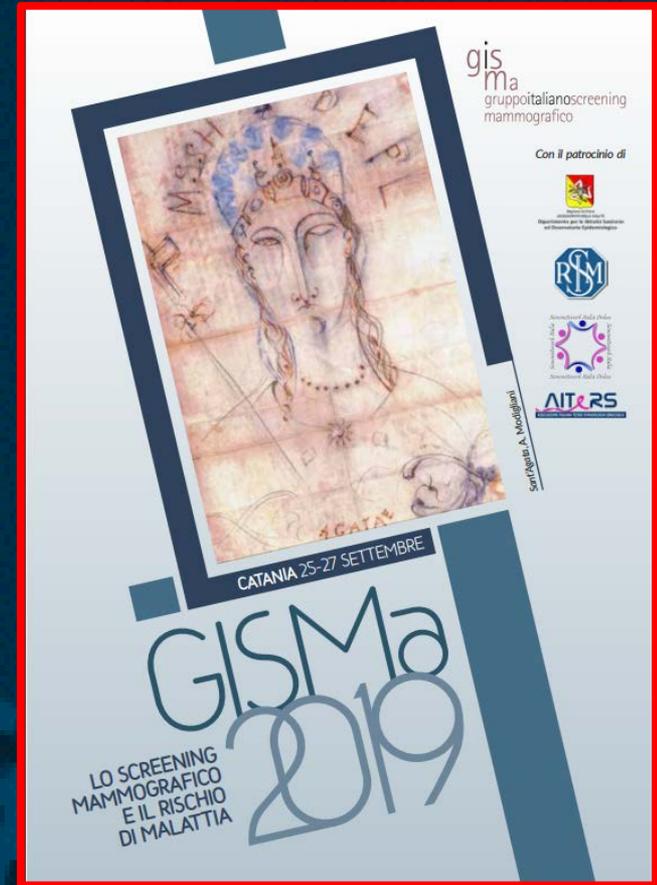


Il trattamento non chirurgico delle lesioni indolenti



Giovanni Mauri,
Division of Interventional Radiology
European Institute of Oncology - Milan, Italy

Interventional Oncology



Medical



Radiation

Oncology

Surgical



Interventional



Image-guided ablations

“Curative” ablation: “A0”

Ablation of the whole tumor volume with a large enough safety margin

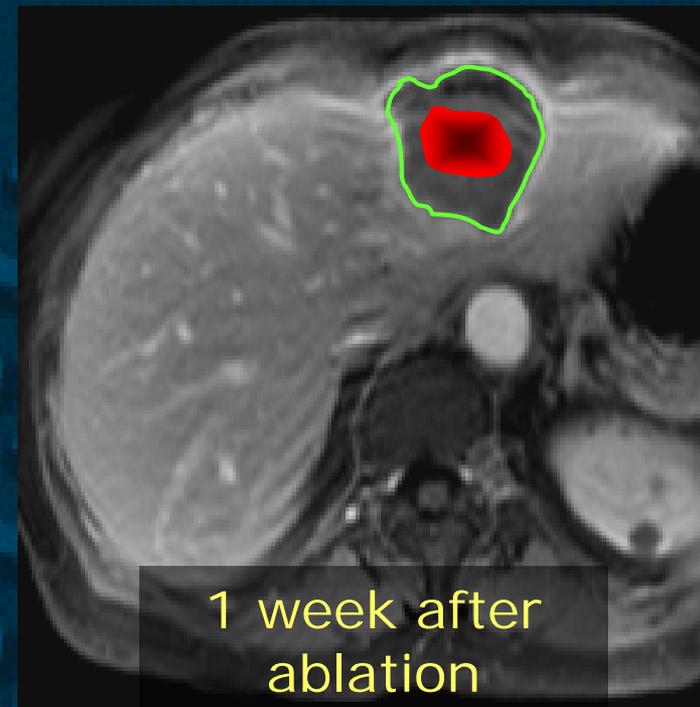
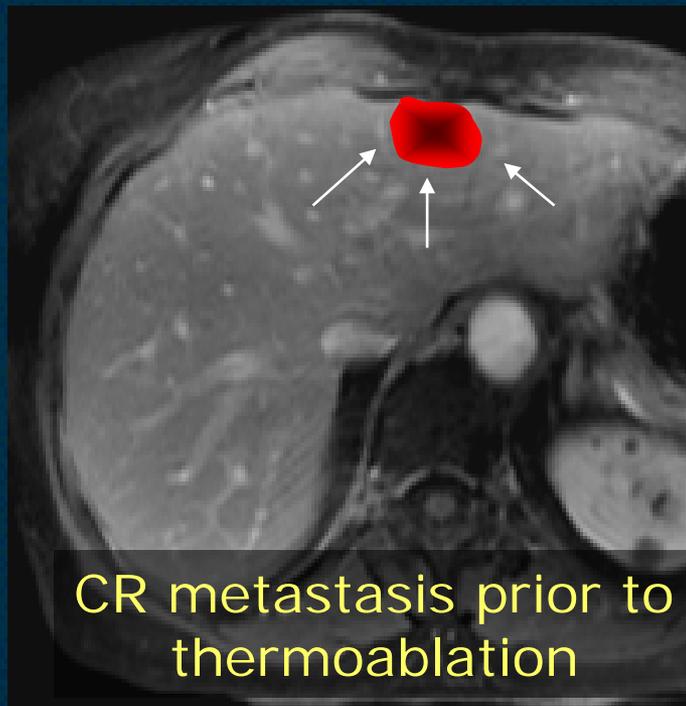


Image-guided ablations

- Recognized effective alternative treatment to surgery in several fields

HCC

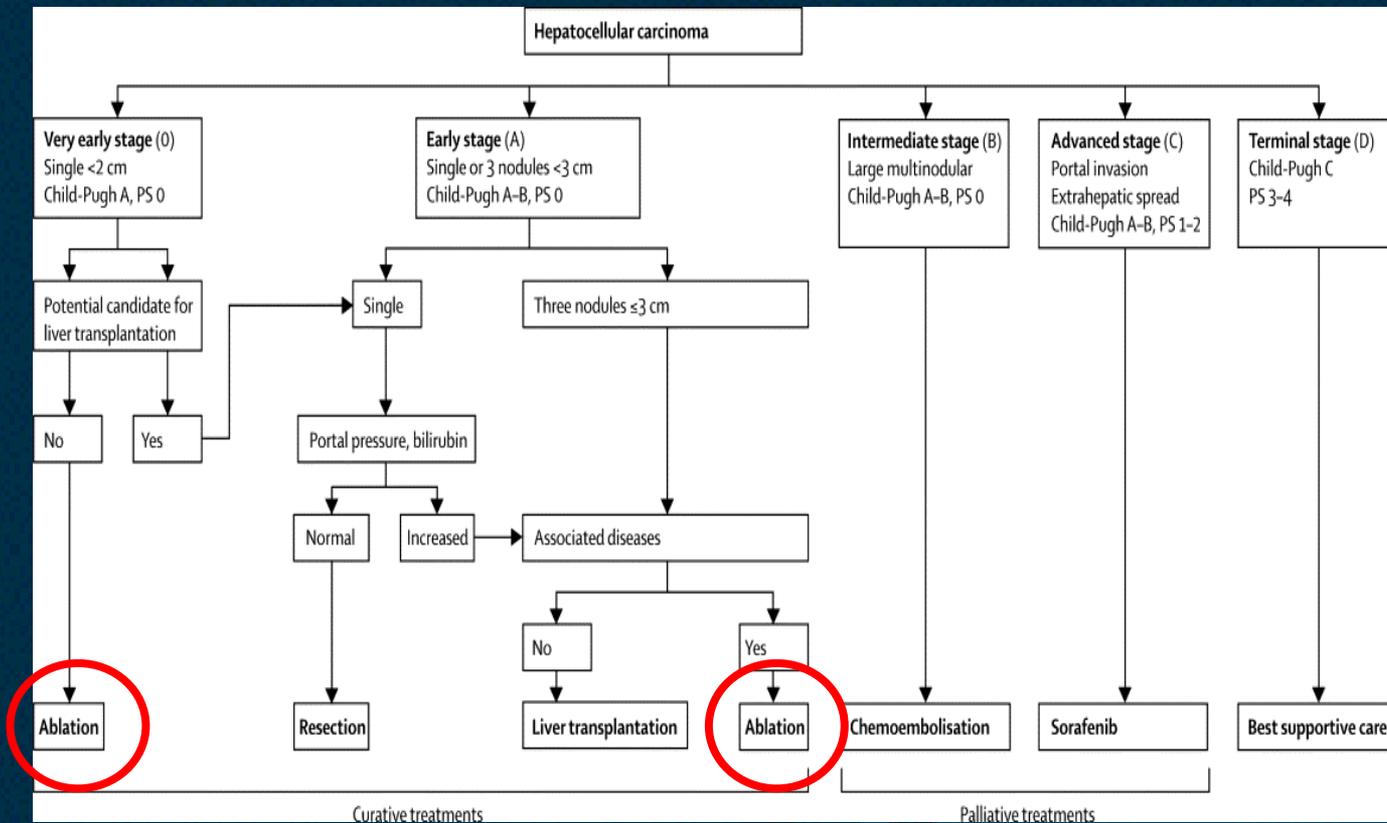


Image-guided ablations

- Recognized effective alternative treatment to surgery in several fields

RCC

Cardiovasc Intervent Radiol. 2014 Apr;37(2):427-37. doi: 10.1007/s00270-014-0846-9. Epub 2014 Jan 31.

Systematic review and meta-analysis of thermal ablation versus surgical nephrectomy for small renal tumours.

Katsanos K¹, Malli L, Krokidis M, McGrath A, Sabharwal T, Adam A.

- Thermal ablation of small renal masses produces oncologic **outcomes similar to surgical nephrectomy** and is associated with significantly **lower overall complication rates** and a significantly less decline of renal function

Radiology. 2008 Jul;248(1):169-78. doi: 10.1148/radiol.2481071448. Epub 2008 May 5.

Radiofrequency ablation versus nephron-sparing surgery for small unilateral renal cell carcinoma: cost-effectiveness analysis.

Pandharipande PV¹, Gervais DA, Mueller PR, Hur C, Gazelle GS.

- RF ablation was preferred over NSS for small RCC treatment at a societal willingness-to-pay threshold level of \$75,000 per QALY.

Image-guided ablations

PROS

- Minimally invasive (no incision less scarring)
- Less pain
- Reduction in mortality, morbidity, hospital stay, cost
- Improved quality of life for cancer patients.
- Improved cosmesis

CONS

- No tissue for pathological examination
 - Complete ablation? Margins? Size? G? PR? ER? HER2?

Rationale for ablation in breast cancer

Mastectomy → Breast Conserving Surgery

Axillary Dissection → Sentinel Node Biopsy

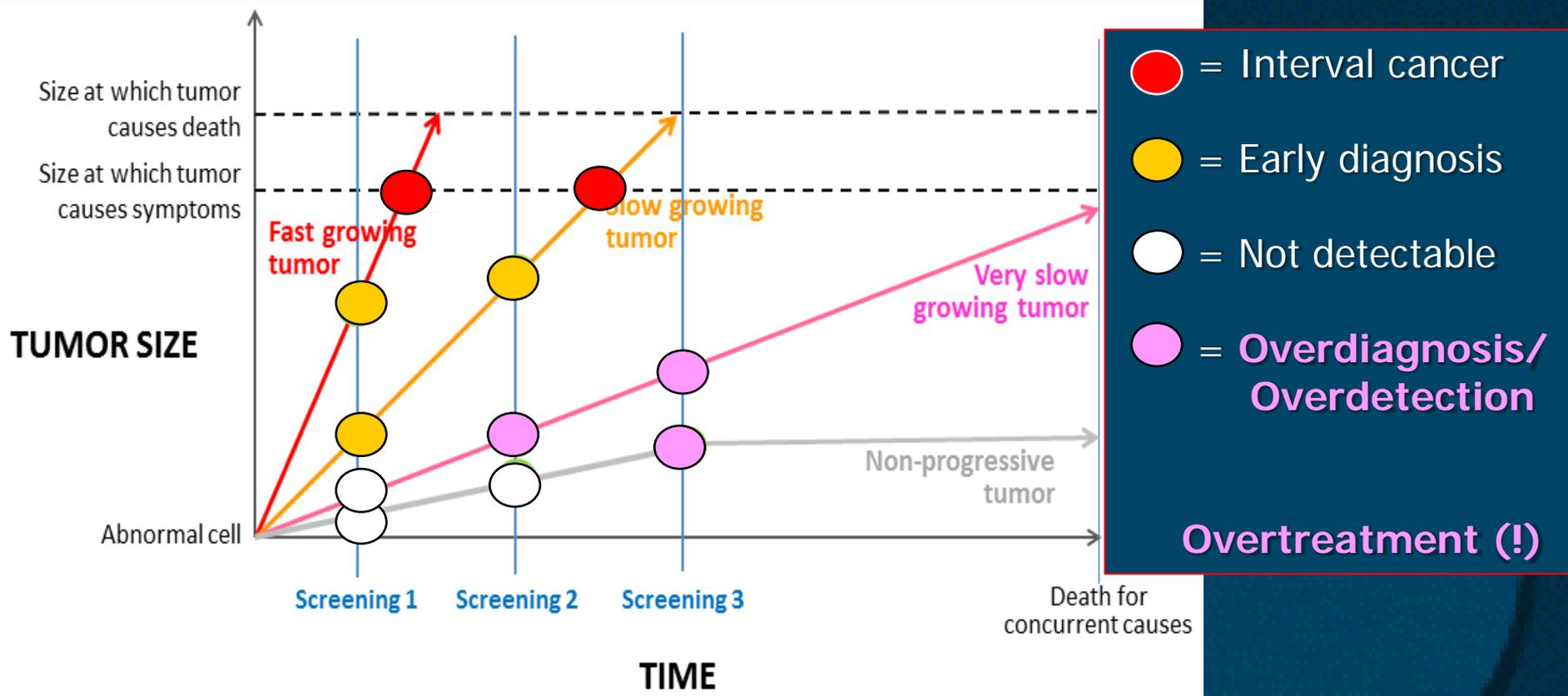
Whole Breast Irradiation → Partial Breast Irradiation

Breast Conserving Surgery
→ *Percutaneous Ablation ??????*

Rationale for ablation in breast cancer

OVERDIAGNOSIS

Detection of a disease (lesion) that will never cause symptoms or death during patient lifetime



ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

ABSTRACT

BACKGROUND

To reduce mortality, screening must detect life-threatening disease at an earlier, more curable stage. Effective cancer-screening programs therefore both increase the incidence of cancer detected at an early stage and decrease the incidence of cancer presenting at a late stage.

METHODS

We used Surveillance, Epidemiology, and End Results data to examine trends from 1976 through 2008 in the incidence of early-stage breast cancer (ductal carcinoma in situ and localized disease) and late-stage breast cancer (regional and distant disease) among women 40 years of age or older.

RESULTS

The introduction of screening mammography in the United States has been associated with a doubling in the number of cases of early-stage breast cancer that are detected each year, from 112 to 234 cases per 100,000 women — an absolute increase of 122 cases per 100,000 women. Concomitantly, the rate at which women present with late-stage cancer has decreased by 8%, from 102 to 94 cases per 100,000 women — an absolute decrease of 8 cases per 100,000 women. With the assumption of a constant underlying disease burden, only 8 of the 122 additional early-stage cancers diagnosed were expected to progress to advanced disease. After excluding the transient excess incidence associated with hormone-replacement therapy and adjusting for trends in the incidence of breast cancer among women younger than 40 years of age, we estimated that breast cancer was overdiagnosed (i.e., tumors were detected on screening that would never have led to clinical symptoms) in 1.3 million U.S. women in the past 30 years. We estimated that in 2008, breast cancer was overdiagnosed in more than 70,000 women; this accounted for 31% of all breast cancers diagnosed.

CONCLUSIONS

Despite substantial increases in the number of cases of early-stage breast cancer detected, screening mammography has only marginally reduced the rate at which women present with advanced cancer. Although it is not certain which women have been affected, the imbalance suggests that there is substantial overdiagnosis, accounting for nearly a third of all newly diagnosed breast cancers, and that screening is having, at best, only a small effect on the rate of death from breast cancer.

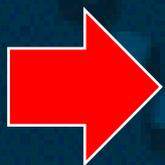
BC diagnosis

Stage	Before Screen.	After Screen.	Delta
Early	112 /100,000	234/100,000	x2
Late	102/100,000	94/100,000	-8%

Overdiagnosis

Past 30 years = 1.3 million

2008 = 70,000 = 31% of all diagnosed BCs



The New York Times

Bleyer and Welch, NEJM, Nov 22, 2012

Rationale for ablation in breast cancer

Thus...

- More BCs detected
 - Smaller cancers detected
 - More overdiagnosis?
 - More overtreatment?
-
- *How counteract a trend for overtreatment?*
 - *Minimally invasive image-guided therapies*

[Int J Hyperthermia](#). 2017 Jun;33(4):489-490. doi: 10.1080/02656736.2016.1262969. Epub 2016 Nov 30.

Image-guided thermal ablation might be a way to compensate for image deriving cancer overdiagnosis.

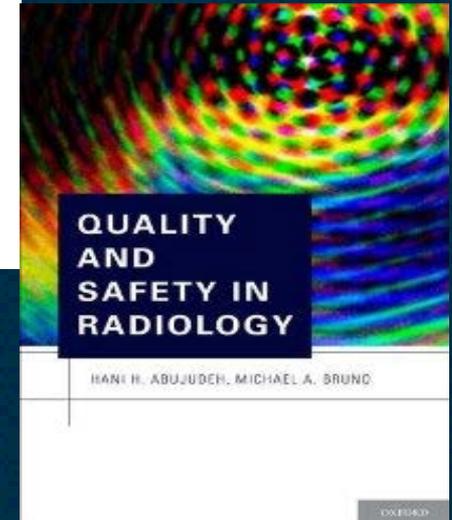
Mauri G¹, Sconfienza LM^{2,3}.

Rationale for ablation in breast cancer

27

Evidence-based Radiology and Its Relationship
with Quality

FRANCESCO SARDANELLI



We cannot have early diagnosis without a rate of overdiagnosis.

No methods, including molecular gene profiling, are available **to stratify cancers** into those to be treated and those not to treat.

Thus, when we find a small cancer, we are compelled to treat it. As a logical consequence, **overdiagnosis causes overtreatment**.

We must minimize the treatment. Interventional radiology can do it.

This is the strong rationale. What's the evidence?

Evidence on ablation in breast cancer

There are several different techniques for image-guided ablations, each one applied in breast tumor treatment

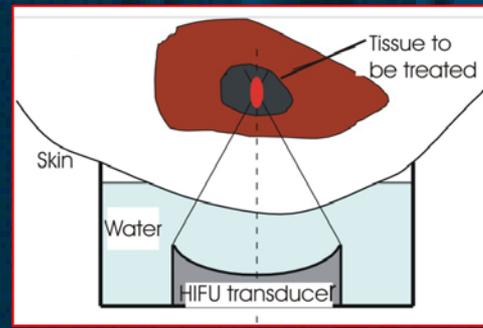
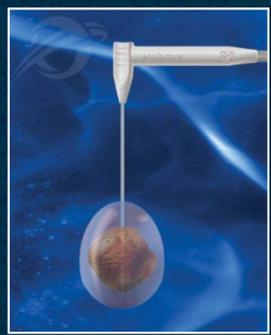
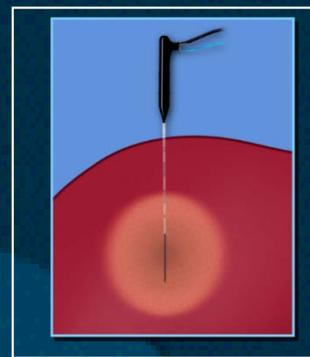
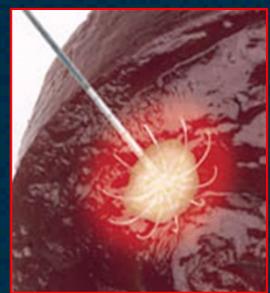
Comparison of thermal ablation techniques for breast cancer.				
Thermal ablation methods	Energy conduction & ablation	Energy delivery through skin	Imaging guidance	Ablation time (varies with tumor size)
Radiofrequency ablation	Heat, not conformal	Percutaneous, with an electrode probe	Ultrasound	10–30 min
Laser ablation	Heat, not conformal	Percutaneous, with an optical fiber	Ultrasound, MRI	25–30 min
Microwave ablation	Heat, not conformal	Percutaneous, with an electrode antenna	Ultrasound	20–60 min
Cryoablation	Cold, not conformal	Percutaneous with an applicator	Ultrasound	15–30 min
HIFU ablation	Heat, conformal	Transcutaneous with no probe insertion	Ultrasound, MRI	30–120 min

Z. Zhao, F. Wu/EJSO 36 (2010) 1149–1155

J Magn Reson Imaging, 2018 Dec;48(6):1479-1488. doi: 10.1002/jmri.26282. Epub 2018 Oct 14.

MRI-guided treatment in the breast.

Pediconi F¹, Marzocca F¹, Cavallo Marincola B¹, Napoli A¹.



Evidence on ablation in breast cancer

Radiofrequency Ablation (RFA)

- high-frequency alternating current from uninsulated tips
- ionic agitation > frictional heating -> thermal coagulation

Radiofrequency Ablation Therapy in Patients with Breast Cancers Two Centimeters or Less in Size

Shoji Oura, Takeshi Tamaki, Issei Hirai, Tatsuya Yoshimasu, Fuminori Ohta, Rie Nakamura, and Yoshitaka Okamura
Department of Thoracic and Cardiovascular Surgery, Wakayama Medical University

- 52 patients
- Tumors 0.5-2.0 cm (mean 1.3)
- Cytological (3-4 weeks) and MRI (1-3 months) assesment

Evidence on ablation in breast cancer



5% glucose injection to protect the skin



gas forming and breast swelling during ablation

Evidence on ablation in breast cancer

- Mean ablation time of 12 minutes (5-25 minutes)
- No patient with viable cancer cells on post-operative cytology

Cosmetics: excellent 83%, good 12%, fair 6%



Conclusions

Safe and good local disease control

Promising alternative to BCS for small BCs

Evidence on ablation in breast cancer

Cryoablation

- Liquid nitrogen or argon gas generate a iceball from the probe tip
- Complete cell destruction can be achieved with two freeze/thaw

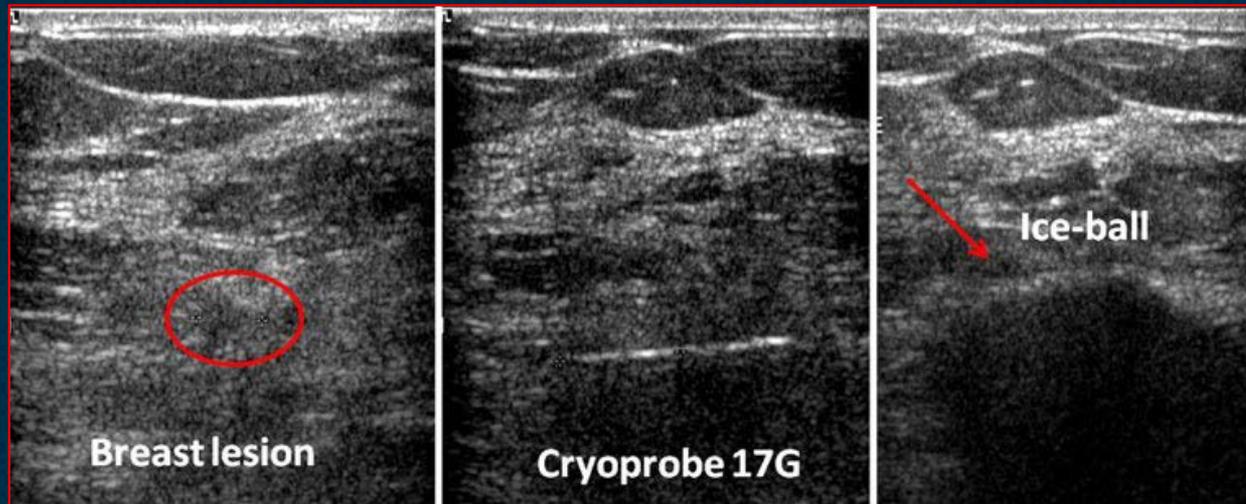
[Eur Radiol](#). 2011 Nov;21(11):2344-53. doi: 10.1007/s00330-011-2179-2. Epub 2011 Jun 17.

Percutaneous local ablation of unifocal subclinical breast cancer: clinical experience and preliminary results of cryotherapy.

[Manenti G](#)¹, [Perretta T](#), [Gaspari E](#), [Pistolese CA](#), [Scarano L](#), [Cossu E](#), [Bonanno E](#), [Buonomo OC](#), [Petrella G](#), [Simonetti G](#), [Masala S](#).

- 15 patients
- Lesion diameter 8 ± 4 mm
- Surgical resection 30-45 days after ablation
- 14/15 (93%) complete ablation

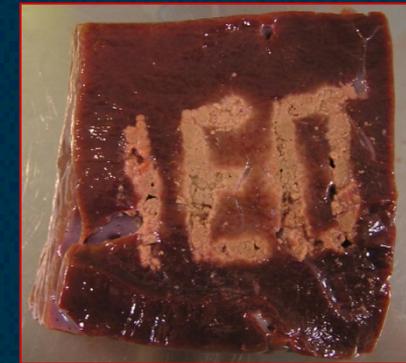
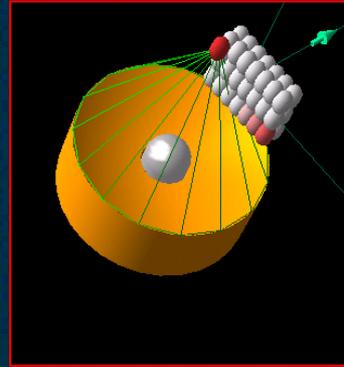
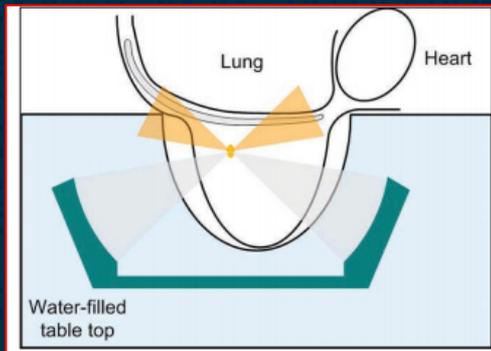
Evidence on ablation in breast cancer



Evidence on ablation in breast cancer

High Intensity Focused Ultrasound (HIFU)

- US/MRI guidance and monitoring
- US energy focused into a small volume converted into heat



“Wide Local Ablation” of Localized Breast Cancer Using High Intensity Focused Ultrasound

FENG WU, MD, PhD,* ZHI-BIAO WANG, MD, PhD, YOU-DE CAO, PhD, XUE-QIANG ZHU, MD,
HUI ZHU, MD, WEN-ZHI CHEN, MD, AND JIANG-ZHONG ZOU, MD

- 23 patients
- Lesion diameter 20-47 mm (mean 31)
- Surgical resection 1-2 weeks after ablation
- 23/23 (100%) complete ablation

Evidence on ablation in breast cancer

[Eur Radiol](#). 2017 Aug;27(8):3199-3210. doi: 10.1007/s00330-016-4668-9. Epub 2017 Jan 3.

Technical success, technique efficacy and complications of minimally-invasive imaging-guided percutaneous ablation procedures of breast cancer: A systematic review and meta-analysis.

[Mauri G](#)¹, [Sconfienza LM](#)^{2,3}, [Pescatori LC](#)⁴, [Fedeli MP](#)⁴, [Ali M](#)⁵, [Di Leo G](#)⁶, [Sardanelli F](#)^{2,6}.

Systematic search (MEDLINE/PubMed, EMBASE, Cochrane Collaboration)

Keywords: HIFU, cryoablation, radiofrequency, microwave, laser, ablation", breast, cancer

Original articles on humans, in English, published since January 1990, enrolling ≥ 10 patients

Search retrieved 688 articles → 613 excluded for Title/Abstract → 75 had full text review

→ 30 discarded → **45 analyzed.**

→ Design: retrospective 2/45 (4%), prospective 43/45 (96%)

Data for all endpoints extracted for only 31 of 45 studies (69%)

Note: no RCT available!

Evidence on ablation in breast cancer

45 studies, 1156 pts. (10-54, **mean 26**), 1167 lesions

	N	Tech.Success ¹	Efficacy ²	Major Compl. ³	Minor Compl. ⁴
RFA	577	96 (93-97)	82 (74-88)	6 (4-9)	7 (4-12)
Laser	227	98 (95-99)	59 (35-79)	4 (2-9)	11 (3-33)
Cryo	156	95 (90-98)	75 (51-90)	2 (1-7)	8 (1-36)
HIFU	129	96 (90-98)	49 (26-74)	10 (5-20)	15 (7-28)
MW	78	93 (81-98)	NA	4 (1-17)	14 (3-46)
Overall 1167		96 (94-97)	75 (67-81)	6 (4-8)	8 (5-13)

Pooled results: % (95% CI)

Not significant differences among techniques except for technique efficacy (p=.009).
Mean lesion size ranged from 11 mm to 31 mm, but tumor size seems not to have impacted on variables (p>.142) (!?)

¹Completed procedure; ²Complete tumor ablation; ³Grade 2-3 burns, necrosis, or pneumothorax; ⁴Local discomfort or grade 1 burns

Evidence on ablation in breast cancer

Imaging-guided ablation of breast cancer showed:

- A high rate of technical success → 96%
- A suboptimal and inhomogeneous efficacy (complete ablation) → only 75%
- A low rate of major/minor complications → 6-8%

Small studies (mean 26 pts!)

Lack of individual data prevented from demonstrating

an effect of tumor size on efficacy

Individual patient data meta-analysis?

few authors accepted...

Evidence on ablation in breast cancer

Radiology. 2018 Nov;289(2):317-324. doi: 10.1148/radiol.2018180235. Epub 2018 Aug 21.

Radiofrequency Ablation Followed by Surgical Excision versus Lumpectomy for Early Stage Breast Cancer: A Randomized Phase II Clinical Trial.

García-Tejedor A¹, Guma A¹, Soler T¹, Valdivieso A¹, Petit A¹, Contreras N¹, Chappuis CG¹, Faló C¹, Pernas S¹, Amselem A¹, Plà MJ¹, Fernández-Montolí E¹, Burdío F¹, Ponce J¹.

Radiofrequency Ablation Followed by Surgical Excision for Early Stage Breast Cancer

Table 2: Pathologic Outcomes

Parameter	RFA Group (n = 20)	Control Group (n = 20)	P Value
Median specimen weight (g)*	42 (24–80)	27 (11–60)	.004
Median specimen volume (mL)*	369 (259–847)	201 (100–602)	.004
Positive margin (intraoperative)	4 (20)	11 (55)	.022
Median tumor size at pathologic examination (mm)*	11.5 (5–20)	10.5 (6–16)	.07
Axillary status			.11
N0	14 (70)	18 (90)	
N1	6 (30)	2 (10)	

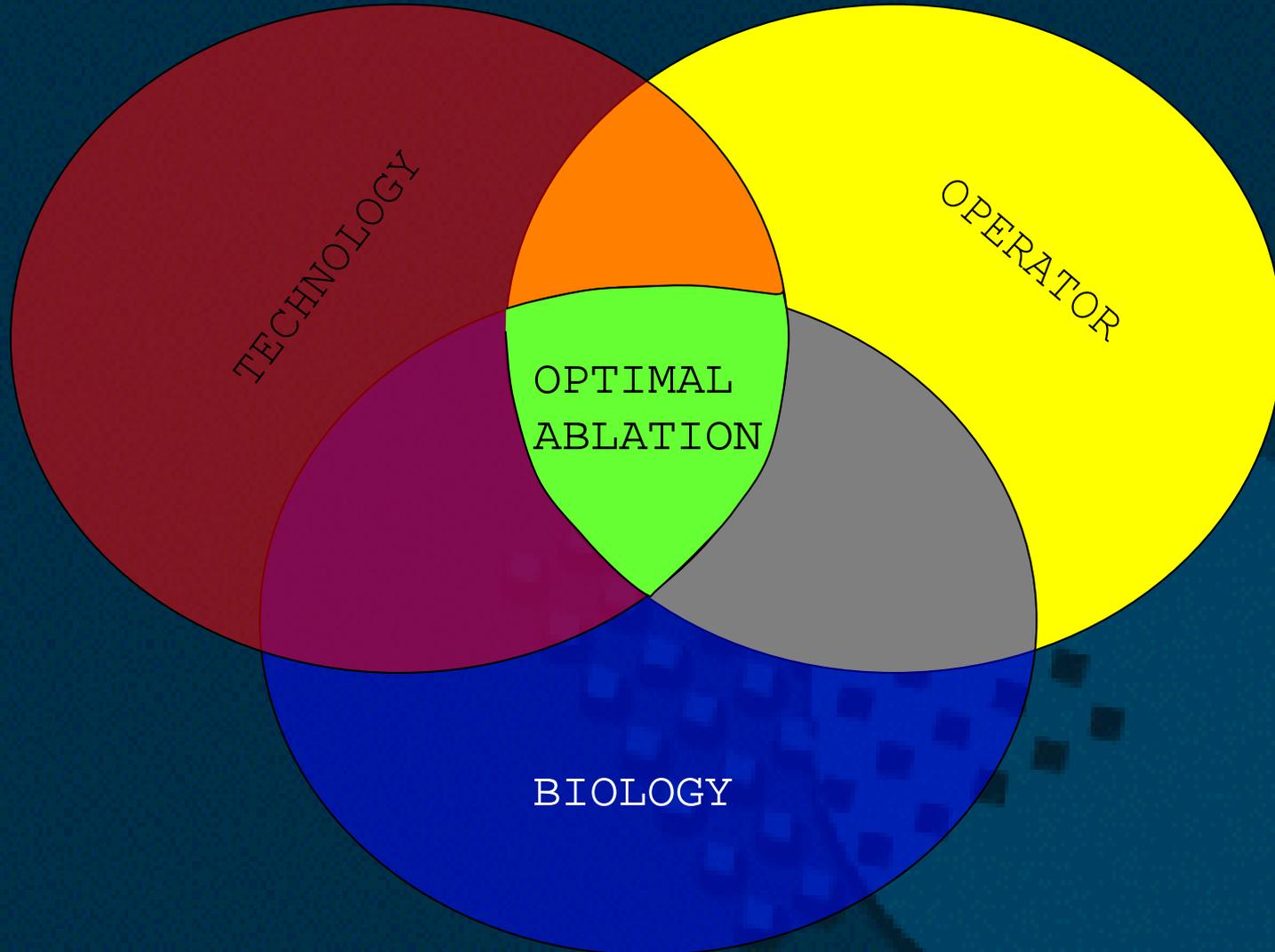
Note.—Unless otherwise indicated, numbers are numbers of participants, with percentages in parentheses. RFA = radiofrequency ablation.

* Numbers in parentheses are the range.

Conclusion: This preliminary study showed that radiofrequency ablation was effective for local tumor control and that tumor-free margins were obtained more often with radiofrequency ablation than with lumpectomy. Surgical excision after radiofrequency ablation was infrequently associated with local infection.

ablation in breast cancer

optimizing tumor ablation



ablation in breast cancer

A STRONG RATIONALE BUT A VERY WEAK EVIDENCE!

WHAT WE NEED?

- Large prospective RCTs image-guided ablation versus surgery
- Experienced operators
- Proper tumor selection
- Preliminary sample size determination
- Non-inferiority design (primary endo-point = local recurrence)
- Secondary end-points: duration, anesthesia, cosmetic results
- Clear cut inclusion criteria (eg, ≤ 2 cm in size)
- High quality pre/post imaging studies (MRI)
- Strict follow-up
- ...Cooperation with surgeons !
- **TO GET A CLEAR EVIDENCE TO BE PRESENTED TO PATIENTS**

ablation in breast cancer

Radiology. 2019 Mar;290(3):849-850. doi: 10.1148/radiol.2019182448. Epub 2019 Feb 5.

Imaging-guided Percutaneous Ablation: A Step Forward to Minimize the Invasiveness of Breast Cancer Treatment.

Mauri G¹, Sconfienza LM^{2,3}, Sardanelli F^{2,4}.

Thank you!!

giovanni.mauri@ieo.it

