

11th B.I.G. of R.A.N.Z.C.R. Meeting
April 05-08, 2017
 Queenstown/New Zealand

MR-guided intervention

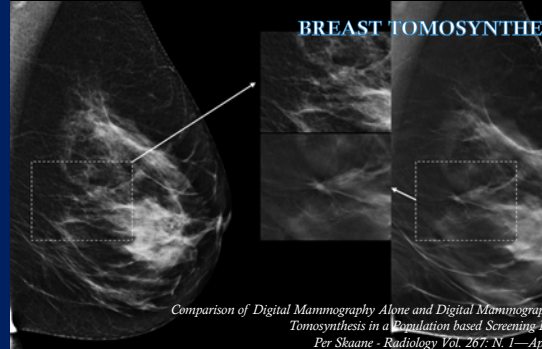
Federica Pediconi
 Department of Radiological, Oncological and Pathological Sciences
 "Sapienza" University of Rome



BACKGROUND

Early diagnosis of breast cancer thanks to technical advances of conventional imaging techniques...

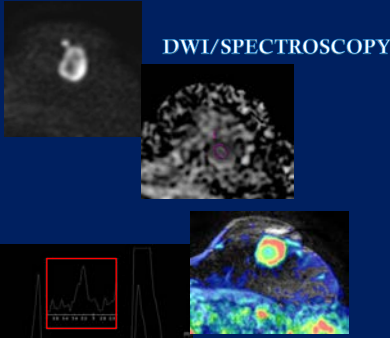
BREAST TOMOSYNTHESIS



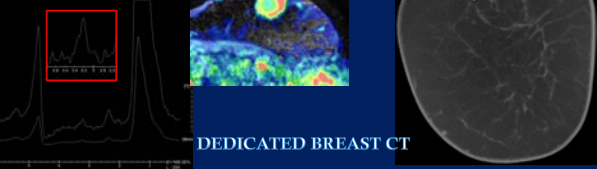
Comparison of Digital Mammography Alone and Digital Mammography Plus Tomosynthesis in a Population based Screening Program
 Per Skaane - Radiology Vol. 267: N. 1—April 2013

...and the introduction of new imaging methods.

DWI/SPECTROSCOPY



DEDICATED BREAST CT




Magnetic Resonance Imaging

Despite in majority of cases MX and US are able to provide the correct diagnosis...

...sometime a lesion can remain hidden until a more accurate examination is performed

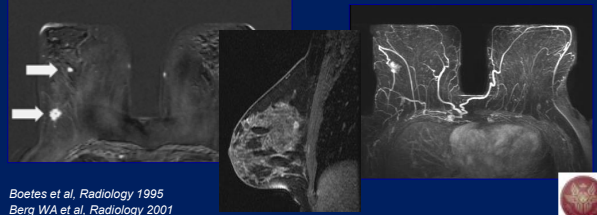
Very small lesion
 Dense Mx
 Inconclusive US scan /second look



Magnetic Resonance Imaging

Breast MR imaging is a highly sensitive technique (94%-100%) for detection of breast cancer.

It can commonly find lesions that are occult on mammograms and US scans



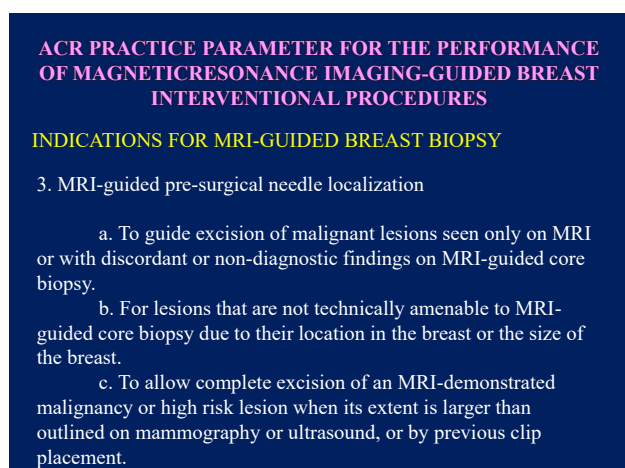
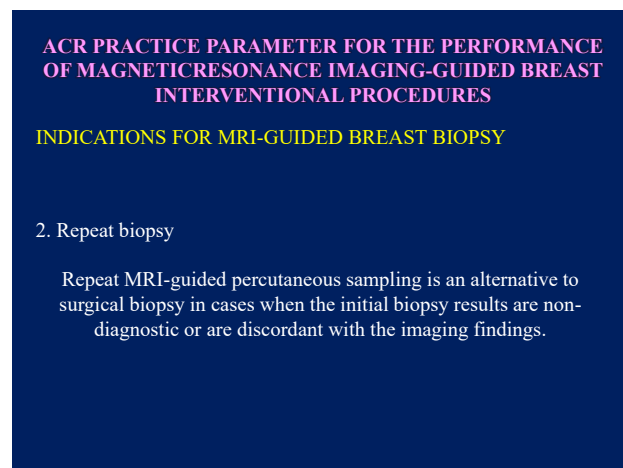
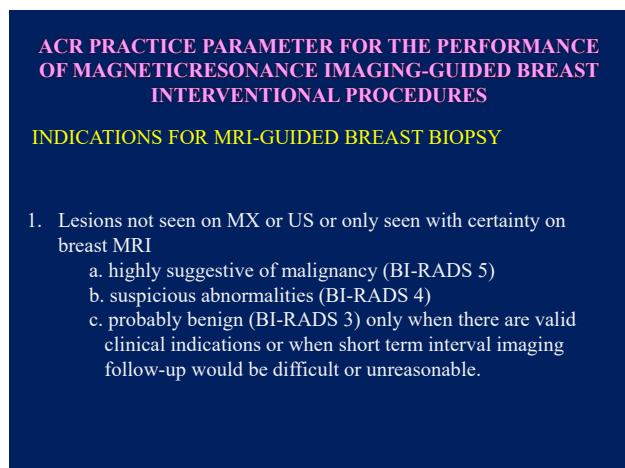
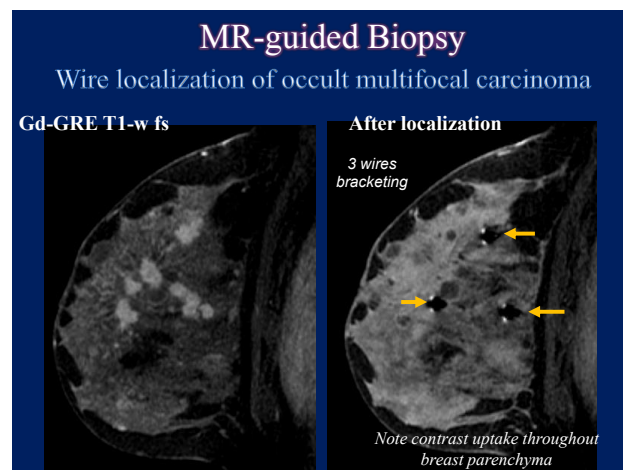
Boetes et al. Radiology 1995
 Berg WA et al. Radiology 2001

Breast Lesions Detected with MR Imaging: Utility and Histopathologic Importance of Identification with US¹

TABLE 1
 Presence of US Correlate versus Lesion Type and Histologic Category in 21 of 93 Lesions

Lesion Characteristics	No. with US Correlate	P Value	Median Size (cm)
Type			
Mass	19/76 (25)	.34	0.8
Nonmass	2/17 (12)		2.9
Histologic type			
Benign	12/74 (16)	.01	0.9
Malignant	9/19 (47)	.35	1.0
DCIS	2/7 (29)		0.9
Invasive	7/12 (58)		1.3

Note.—Numbers in parentheses are percentages.



NON-INVASIVE ABLATION

Several publications focusing on new non-invasive approaches for breast cancer treatment

DIFFERENT WAYS TO ABLATE TISSUE

- ✓ Interstitial Laser Therapy (ILT)
- ✓ RadioFrequency Ablation (RFA)
- ✓ High Focused Ultrasound (HIFU)

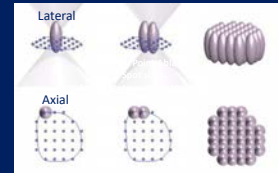
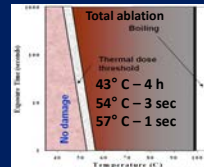
✓ Cryotherapy

cause tissue necrosis by increasing the temperature

causes tissue necrosis by a rapid temperature decrease

HIGH-INTENSITY FOCUSED ULTRASOUND

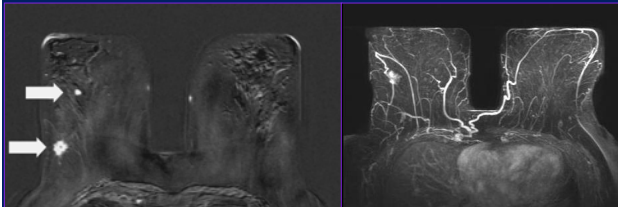
A high-energy focused ultrasound beam rapidly generate a substantial increase in local tissue temperatures ($>60^{\circ}$) by converting acoustic energy into heat. Consequences are protein denaturation and coagulation necrosis of target tissue with no damage to surrounding structures.



MAGNETIC RESONANCE

Technique of choice for breast cancer imaging

- Higher accuracy compared to mammography and US
- Better evaluation of tumor shape and dimensions
- Depiction of synchronous lesions
- Details on neo-angiogenesis
- Best imaging technique for the evaluation response of non-invasive procedures



MRgFUS

- MRI-guided focused ultrasound (MRgFUS) is a noninvasive thermal ablation method that uses magnetic resonance imaging (MRI) for target definition, treatment planning, and control of energy deposition.
- Integrating FUS and MRI as a therapy delivery system allows to localize, target, and monitor in real time, and thus to ablate targeted tissue without damaging normal structures.

MR guided Focused Ultrasound

Technical aspects and patient positioning

MR-GUIDANCE ADVANTAGES

1. High contrast resolution on three planes

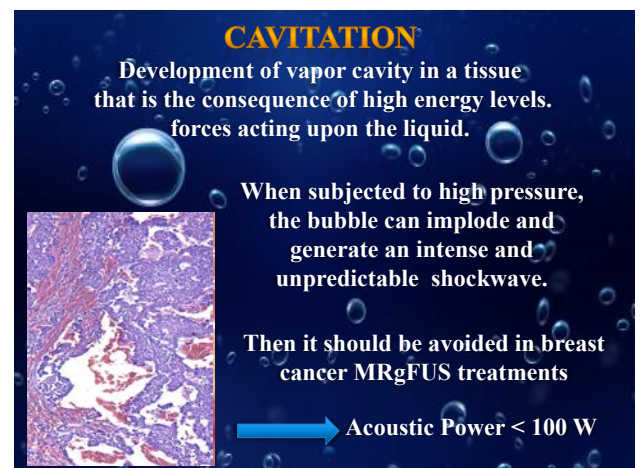
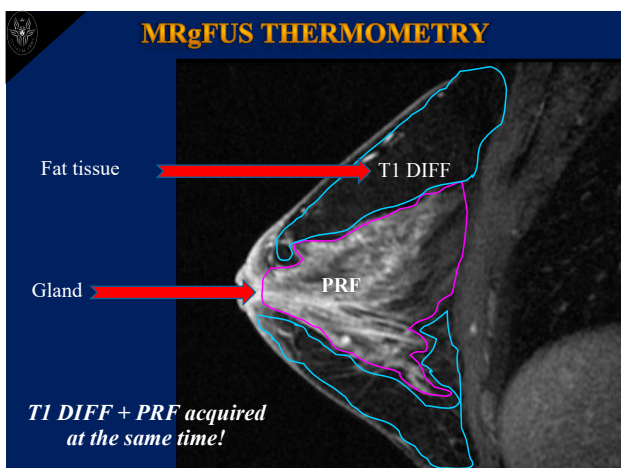
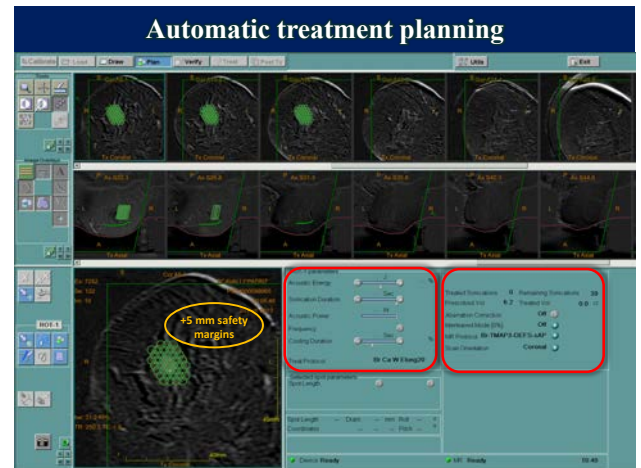
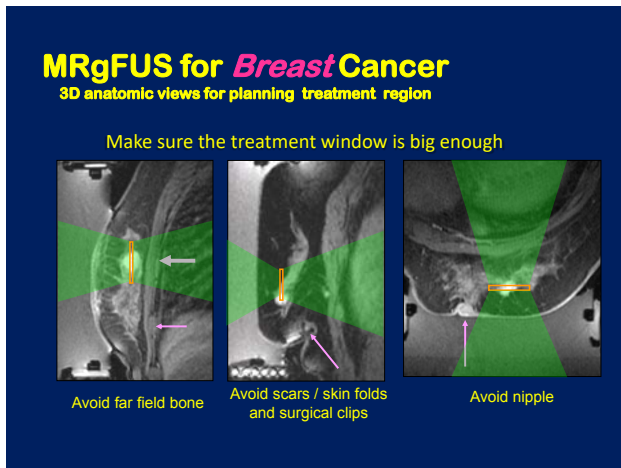
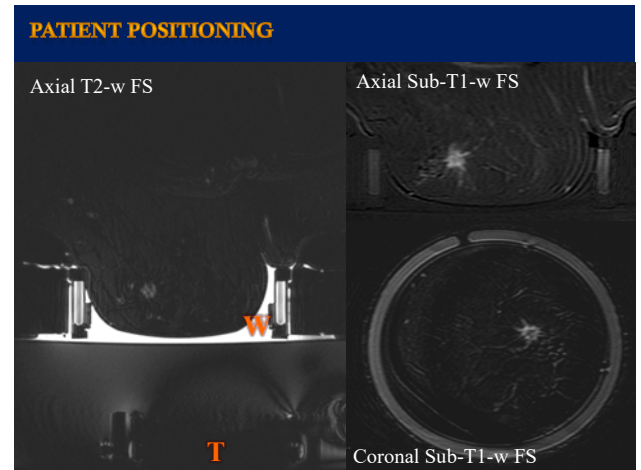
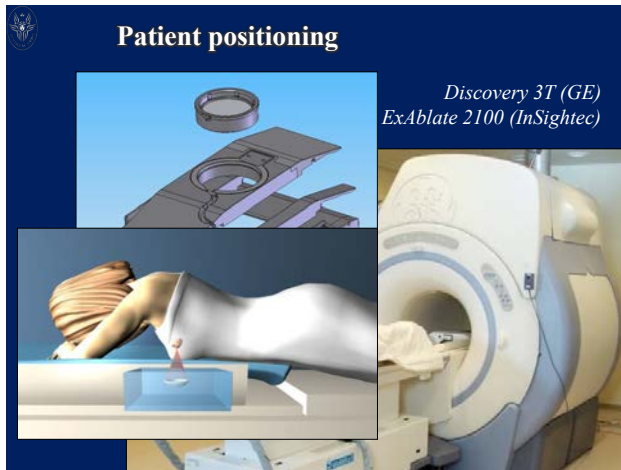
→ lesion depiction and treatment planning

2. Real-time temperature monitoring

→ evaluation of thermal damage

3. Visualization of US-beam

→ patient safety



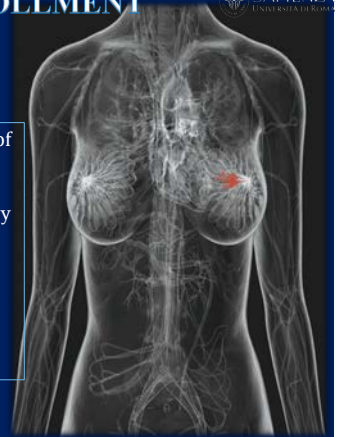
MR guided Focused Ultrasound

Personal Experience

Pt ENROLLMENT

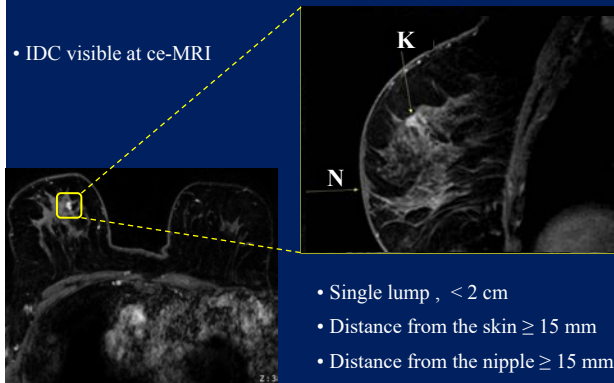
12 patients

- Biopsy-proven single focus of Invasive Ductal Carcinoma.
- No personal or family history suggesting BRCA1/2 gene mutation.
- No evidence of suspicious axillary lymph nodes at imaging.



MRGFUS TECHNIQUE - INCLUSION CRITERIA -

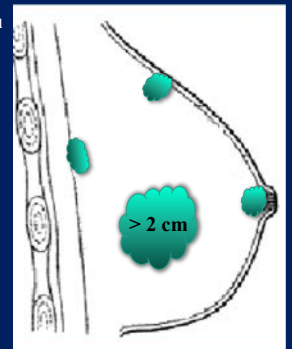
- IDC visible at ce-MRI



- Single lump, < 2 cm
- Distance from the skin ≥ 15 mm
- Distance from the nipple ≥ 15 mm

MRGFUS TECHNIQUE - EXCLUSION CRITERIA -

- Invasive lobular carcinoma, in situ ductal carcinoma (microcalcifications)
- Non-accessible lesions
- Breast implants
- Ca intolerance
- MR non-compatible devices
- Claustrophobia and position



STUDY PROTOCOL

Fat-sat Ax T2-weighted TSE
Fat-sat T1 3D GRE at least on 2 planes

Gd injection

Fat-sat T1 3D GRE on the same planes
→ subtracted images

DEPICTION OF LESION
DIMENSIONS AND
BORDERS

FUS Treatment

Fat-sat Ax T2-weighted TSE
Fat-sat T1 3D GRE at least on 2 planes

Gd injection

Fat-sat T1 3D GRE on the same planes
→ subtracted images

EVALUATION OF
TREATMENT EFFICACY

STUDY PROTOCOL

MRI
+
Histopathology

MRgFUS

24h-Clinical
Follow-up

10-21 days MRI
Follow-up

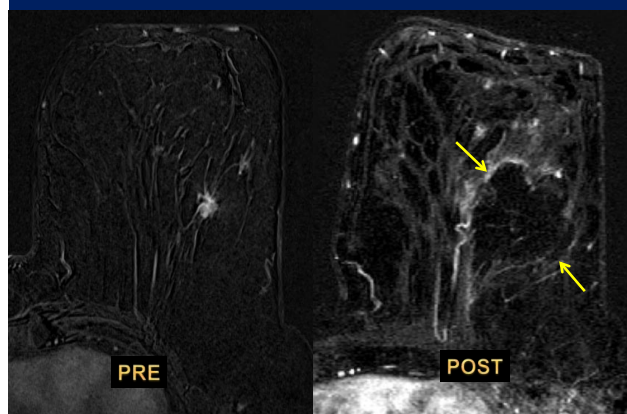
Surgery

1 day

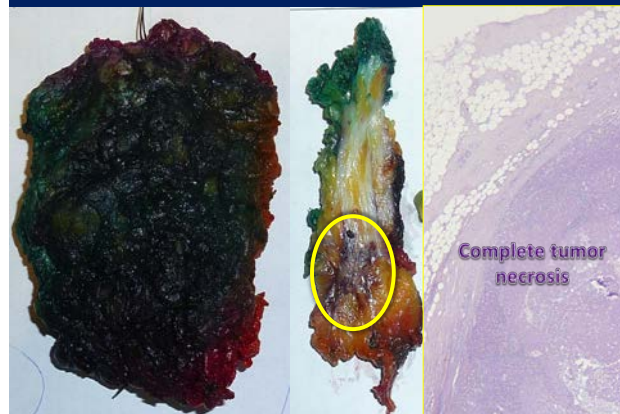
10-21 days

≤ 14 days

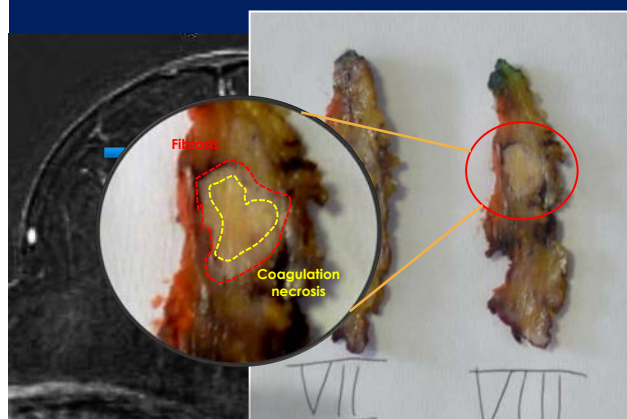
F, 53 yo, left breast IDC



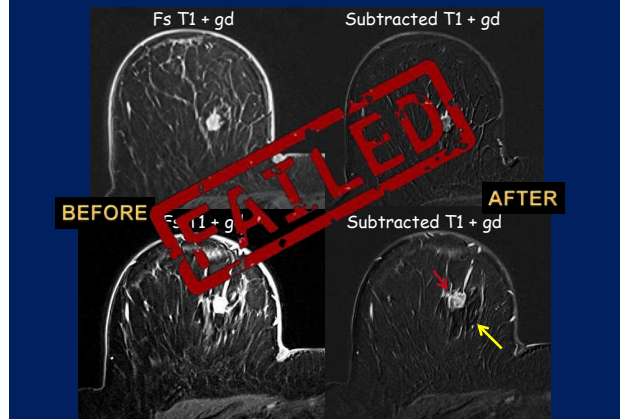
F, 48 yo, left breast IDC



F, 52 yo, left breast IDC



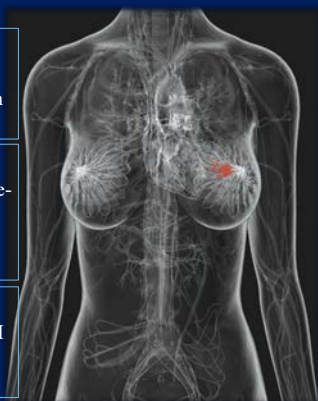
F, 60 yo – Right breast IDC - T1 N0 M0



RESULTS

12 patients


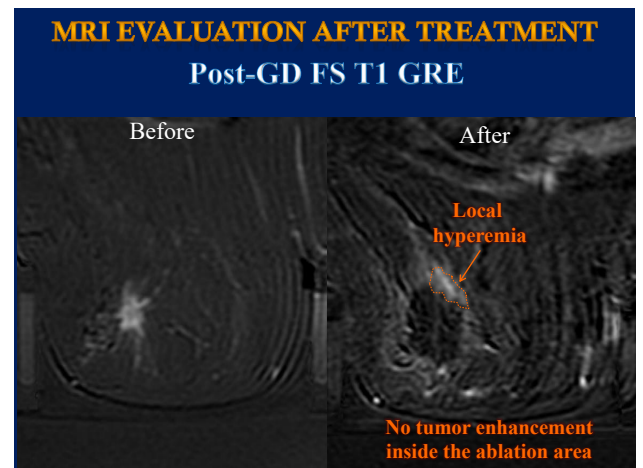
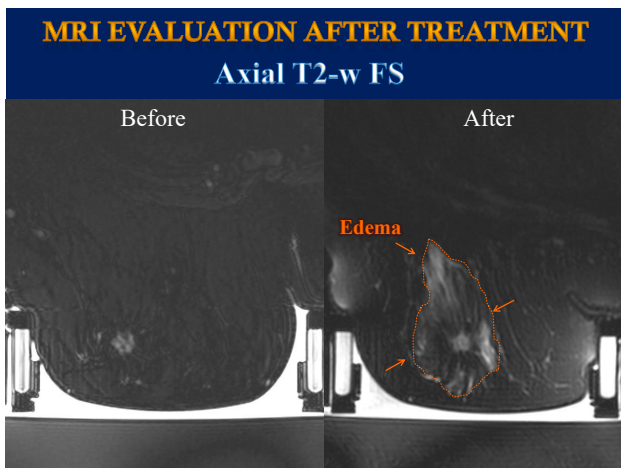
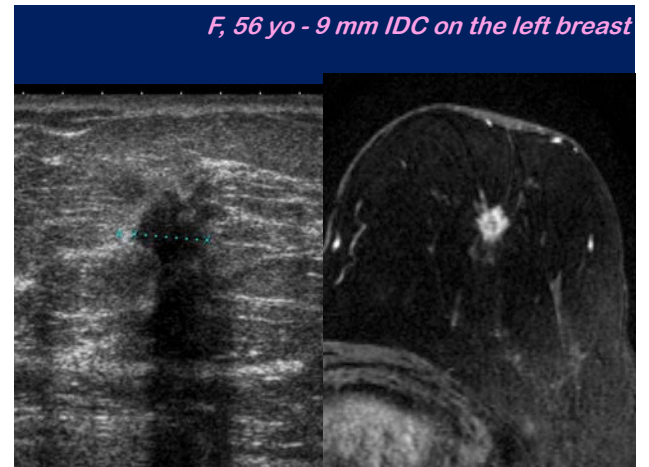
- 8 patients**
 - No enhancement at ce-MRI
 - At histopathology: coagulation necrosis, hemorrhage, fibrosis
- 2 patients**
 - Residual enhancing tissue at ce-MRI
 - Viable cells confirmed at histopathology
- 2 patients**
 - No enhancing tissue at ce-MRI
 - Small foci of tumoral cells visible at histopathology



PATIENT MANAGEMENT

Patient may feel:

- ✓ Skin heat
- ✓ Heat during sonication
- ✓ Rib discomfort/pain
- ✓ Discomfort due to prone position

RESULTS FROM THE LITERATURE

J Vasc Interv Radiol. 2003 Oct;14(10):1275-82.
Feasibility of magnetic resonance imaging-guided focused ultrasound surgery as an adjunct to tamoxifen therapy in high-risk surgical patients with breast carcinoma.
Granfelice D¹, Khiat A, Boulanger Y, Amara M, Belbidia A.

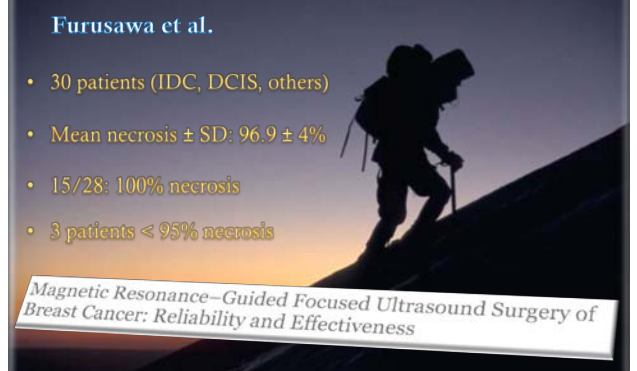
<ul style="list-style-type: none"> 24 patients NO SURGERY (high risk or refused) Possibility of 2° treatment FU with imaging and biopsy 	<ul style="list-style-type: none"> Absence of MR enhancement 1 minor complication 19/24 negative biopsy 3/5 residual tumor
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RESULTS FROM THE LITERATURE

2006
Furusawa et al.

- 30 patients (IDC, DCIS, others)
- Mean necrosis \pm SD: 96.9 \pm 4%
- 15/28: 100% necrosis
- 3 patients \leq 95% necrosis

Magnetic Resonance-Guided Focused Ultrasound Surgery of Breast Cancer: Reliability and Effectiveness



RESULTS FROM THE LITERATURE

Study	Patients	Outcome of the ablation procedure
1. Miyazawa et al. (2001) [45]	11	- Fibroadenomas - No surgical resection - Eight lesions (72%) demonstrated complete or partial lack of contrast uptake (necrosis) - Three lesions (27%) showed no marked decrease of contrast uptake (false)
2. Shih et al. (2001) [46]	4	- Invasive ductal carcinoma (n=1) - Complete necrosis in four lesions (100%) - In the treated part of the tumor, cells were partly necrotic and nearly unrecognizable - No exact percentage is provided
3. Giordano et al. (2001) [47]	17	- Invasive ductal carcinoma (n=14) - Adenocarcinoma (n=3) - Subcutaneous lobular carcinoma (n=1) - All tumors <1.5 cm in size - Breast neoplasms, not specified - All tumors <1.5 cm in size
4. Giordano et al. (2001) [48]	24	- Invasive ductal carcinoma (n=11) - Adenocarcinoma (n=13) - Complete necrosis in four lesions (36%) - Low heat 10% residual tumor in nine lesions (37%) - Residual 30-50% residual tumor in four lesions (17%) - No surgical resection - Complete necrosis after 1 or 2 treatments (14 lesions (58%)) - Residual tumor after two treatments (false) in 5 lesions (21%)
5. Giordano et al. (2001) [49]	32	- Invasive ductal carcinoma (n=11) - Adenocarcinoma (n=11) - All tumors <1.5 cm in size - Breast neoplasms, not specified - All tumors <1.5 cm in size
6. Zipp et al. (2001) [50]	18	- Invasive ductal carcinoma (n=11) - Infiltrating lobular carcinoma (n=1) - All tumors <1.5 cm in size - Breast neoplasms, not specified - All tumors <1.5 cm in size
7. Kiser et al. (2000) [51]	36	- Invasive ductal carcinoma (n=25) - Infiltrating lobular carcinoma (n=11) - All tumors <1.5 cm in size - Breast neoplasms, not specified - All tumors <1.5 cm in size
8. Furusawa et al. (2007) [47]	38	- Invasive ductal carcinoma (n=28) - Ductal carcinoma in situ (n=7) - Invasive mucinous carcinoma (n=1) - Complete necrosis in 20 lesions (53%) - Complete necrosis in 15 lesions (39%)
9. Furusawa et al. (2007) [47]	21	- Breast neoplasms, not specified - All tumors <1.5 cm in size - Low heat 97% necrosis in three lesions (15%) - No surgical resection - Mean follow-up 14 months (range 3-26 months) - Complete necrosis in 20 lesions (95%) - One recurrence (5%)

9 Furusawa et al. (2007) [47] 21

- Breast neoplasms, not specified
- All tumours <5 cm in size

- No surgical resection

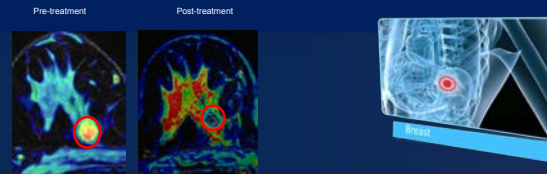
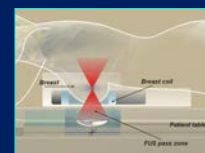
- Mean follow-up 14 months (range 3-26 months)

- Complete necrosis in 20 lesions (95%)

- One recurrence (5%)

RESULTS Breast

- Non-invasive alternative to surgical "lumpectomy"
- Ambulatory, single session procedure
- Over 300 patients treated in Phase I/II trials, up to 48 months follow-up
- Patients treated with MRgFUS, followed by adjuvant therapy
- No recurrences; no severe adverse events



SAPIENZA
UNIVERSITÀ DI ROMA

SOME CONSIDERATIONS...

ORIGINAL ARTICLE

Breast Focused Ultrasound Surgery With Magnetic Resonance Guidance

Eva C. Gombos, MD,* Daniel F. Kacher, MS,* Hidemi Furusawa, MD,† and Kiyoshi Namba, MD†

1) Need for pre-treatment biopsy with immunochemistry

enhanced MRI must replace histopathology. As no additional tissue is obtained, the histological diagnosis and tumor markers (estrogen and progesterone receptor status and HER2-Neu status) must be determined from the pretreatment core biopsy. Additional tissue can be taken at core biopsy for

Magnetic resonance thermal monitoring may be challenging in a breast that is of predominantly fatty composition.³⁹ Proton resonance frequency shift techniques work in aqueous tissue, but not in fatty tissue. Moreover, subtraction-

2) Difficult thermometry in fatty breasts.

There is a possibility of residual viable cancer cells with MRgFUS; however, residual tumor is a frequent finding with surgical removal and reexcision: in 50% or more of lumpectomies, the margins are inadequate, involved, or close. Histopathologic studies also demonstrated that histologically negative or close biopsy margins do not guarantee complete excision.^{39,40}

3) Possibility of incomplete ablation.

SOME CONSIDERATIONS...

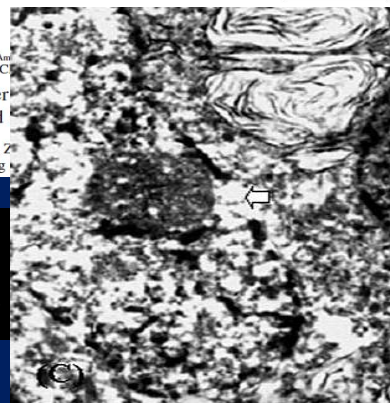


Excerpta Medica

Heat fixation of cancer ultrasound

Feng Wu, M.D., Ph.D.,^{a,*} Zhong-Lin Xu, M.D.,^b Qiang

The use of electronic microscopy and NADH-diaphorase demonstrated no viability in those cells.



A RECENT REVIEW OF LITERATURE...

Lupatkin Radiology
pp 1-12

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

Authors:

Giovanni Mauri, Luca Maria Sconfienza, Lorenzo Carlo Pescatori, Maria Paula Fedeli, Marco Ali, Giovanni Di Leo, Francesco Santarelli

Forty-five studies were analysed, including 1,156 patients and 1,168 lesions.

Radiofrequency, microwaves, laser, cryoablation and high-intensity focused ultrasound were used.

Mauri, G., Sconfienza, L.M., Pescatori, L.C. et al. Eur Radiol (2017).

A RECENT REVIEW OF LITERATURE...

Results:

- Pooled technical success was 96%** (95%CI 94–97%)
[laser=98% (95–99%); HIFU=96% (90–98%); radiofrequency=96% (93–97%); cryoablation=95% (90–98%); microwave=93% (81–98%)].

- Pooled technique efficacy was 75%** (67–81%)
[radiofrequency=82% (74–88); cryoablation=75% (51–90); laser=59% (35–79); HIFU=49% (26–74)].

- Major complications pooled rate was 6%** (4–8).
- Minor complications pooled rate was 8%** (5–13%).

Mauri, G., Sconfienza, L.M., Pescatori, L.C. et al. Eur Radiol (2017).

A RECENT REVIEW OF LITERATURE...

Conclusions:

Imaging-guided percutaneous ablation techniques of breast cancer have a high rate of technical success, while technique efficacy remains suboptimal.

Key Points:

- Imaging-guided ablation techniques for breast cancer are 96% technically successful.
- Overall technique efficacy rate is 75% but largely inhomogeneous among studies.
- Overall major and minor complication rates are low (6–8%).

Mauri, G., Sconfienza, L.M., Pescatori, L.C. et al. Eur Radiol (2017).

CONCLUSIONS

- ✓ Valid alternative to conservative surgery
- ✓ Non-invasive, incisionless, safe
- ✓ Conscious sedation, no hospitalization nor general anesthesia
- ✓ No ionizing radiations
- ✓ Well tolerated, rapid return to normal daily activities for the patient
- ✓ Improvement in quality of life

