ABLATIVE THERAPY FOR BREAST TUMORS

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LUMPECTOMY FOR SMALL BREAST TUMORS

- Brief outpatient procedure
- Low morbidity, rare mortality
- Local anesthesia ± sedation
LUMPECTOMY FOR SMALL BREAST TUMORS

- Local Control ~ 93% of patients
- Cosmesis good/excellent ~ 90% of patients

- Gold standard
- Bar is very high
SURGERY vs ABLATION

Surgery

Transcutaneous Ablation

GONE

GONE

ABLATION OF BREAST TUMORS

• Minimally or Non-invasive therapy
• Real-time image guidance
• Ambulatory, single session
• Conscious sedation, no G.A.
• Extremely low morbidity
• Better cosmesis
• Percutaneous
  – Skin is traversed by a probe or needle
• Transcutaneous
  – Energy passes harmlessly through the skin

• Percutaneous Ablation
  – Skin is traversed by a probe or needle
• Transcutaneous
  – Energy passes through the skin
ABLATIVE BREAST TUMOR THERAPY

- Percutaneous
  - Laser
  - Cryoablation
  - Percutaneous microwave
  - Radiofrequency

INTERSTITIAL LASER THERAPY

- Fiber optic cable and temp probe
- Guidance
  - MRI
  - US
  - X-Ray (Stereotactic)
- 60 degrees Celsius
INTERSTITIAL LASER THERAPY

• Dowlatshahi et al. 2002 – treat and excise
  – 54 cancers
    » Stereotactic guidance
    » 70% of cases complete ablation on excision

• ABLATE - fibroadenoma
  – American Breast Laser Ablation Therapy Evaluation


ABLATIVE BREAST TUMOR THERAPY

• Percutaneous
  – Cryoablation
  – Percutaneous microwave
  – Radiofrequency
## CRYOABLATION

- **1-2 mm probe(s) placed through skin**
  - US guidance
  - CT guidance
- **Freeze and thaw**
  - 1, 2, or 3 cycles
- **+/− sedation or anesthesia**

<table>
<thead>
<tr>
<th>US</th>
<th>CT</th>
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<tr>
<td>![US Image]</td>
<td>![CT Image]</td>
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Cryoablation

- Cazzato et al. 2015
  - n= 23, “unsuitable for surgery”
  - Median age 85 yrs
  - Treat and observe study
  - Mean tumor size = 14 mm
  - Combined US/CT guidance

CRYOABLATION

- 2-3 cycles, with min. 1cm "margin" +/- local and sedation
  - 23/23 completed treatment
  - 1 patient with frostbite
- No radiation therapy
- 5 local recurrences (14.6 months)

- Poplack et al. 2015
- Treat and excise study
  - MRI at 1 month, then excision
- n = 20, all patients completed tx.
- Ice ball 2x lesion radius + 2cm
- No anesthesia or sedation
• No frostbite
• 17/20 (85%) pts had no residual dz. at surgery
• MRI
  – poor sensitivity to detect residual dz. (0%)

• ACOSOG – Z1072
• n = 99 (87 evaluable)
  – Treat, MRI image, and excise study
    » US guidance
    » 60/87 (69%) complete ablation
    » MRI negative predictive power = 75%
CRYOABLATION + IMMUNOTHERAPY

- Cryoablation + ipilimumab (ipi)
  - 19 patients
    » 7 cryoablation only followed by surgery
    » 6 ipi only followed by surgery
    » 6 cryoablation + ipi, followed by surgery
- Cryoablation +/- ipilimumab
  » Increased newly expanded T-cell clones

Page, et al. ASCO Annual Meeting 2014, Abs #3021 Chicago, IL.

ABLATIVE BREAST TUMOR THERAPY

- Percutaneous
  - Laser
  - Cryoablation
  - Percutaneous microwave
  - Radiofrequency
PERCUTANEOUS MICROWAVE ABLATION

- Zhiu et al, 2012 treat and excise study
  - 43 patients (41 treated)
    » Tumors < 3cm
    » US guided
  - General anesthesia
  - Treatment time < 5 min

Radiology: Volume 263: Number 2—May 2012

PERCUTANEOUS MICROWAVE ABLATION

- Complete ablation in 37/41 (90%) by alpha-NADH-diaphorase-staining
- 1 Skin burn

Radiology: Volume 263: Number 2—May 2012
ABLATIVE BREAST TUMOR THERAPY

• Percutaneous
  – Laser
  – Cryoablation
  – Percutaneous microwave
  – Radiofrequency

RADIOFREQUENCY ABLATION

• Over 30 published breast tumor treatment studies
  – n = 3 to 52 pts
  – Tumors < 2cm
  – 50 – 100% complete ablation
  – 5% skin burns, or “chronic fistulas”
Breast Cancer

• Percutaneous
  – Skin is traversed by a probe or needle
• Transcutaneous Ablation
  – Energy passes through the skin
TRANSCUTANEOUS ABLATION OF BREAST TUMORS

• Focused Microwave Thermotherapy
• Focused ultrasound ablation
  – ultrasound guidance
  – MRI guidance

FOCUSED MICROWAVE THERMOTHERAPY

• Ultrasound guidance
• H$_2$O content of tumor vs fat
  – 19% in fatty breast tissue
  – 74% in breast cancer
• Four clinical trials
  – Both large and small tumors
FOCUSED MICROWAVE THERMOTHERAPY

• Multicenter, randomized study
• 75 evaluable cancer pts, BCT
• FMT followed by surgery vs surgery only
  – Mean tumor size was 1.7cm
  – 34 in the FMT + surgery arm


FOCUSED MICROWAVE THERMOTHERAPY

• 34 in the FMT + surgery arm
  – mean necrosis by volume was 30%
  – 3/34 (9%) skin burns
  – 8/34 (24%) mod/intolerable discomfort

FOCUSED MICROWAVE THERMOTHERAPY

• Results have been mixed
  – efficacy
  – tolerability

TRANSCUTANEOUS ABLATION OF BREAST CANCER

• Focused microwave thermotherapy
• Focused ultrasound ablation
  – ultrasound guidance
  – MRI guidance
FOCUSED ULTRASOUND ABLATION

Magnifying glass

Sun
FOCUSED ULTRASOUND ABLATION

Parallel to the Beam Path

Perpendicular to the Beam Path

Illustration

FOCUSED ULTRASOUND ABLATION
FOCUSED ULTRASOUND ABLATION

TRANSCUTANEOUS ABLATION OF BREAST CANCER

- Focused ultrasound ablation
  - ultrasound guidance
  - MRI guidance
US-GUIDED FOCUSED ULTRASOUND ABLATION

• 23 patients with breast cancer < 6cm
  – USgFUSA, followed by excision
    » 23/23 complete necrosis
    » 1 (3%) skin burn
    » Excellent cosmesis

Wu, et al British J of Cancer 2003, 89;2227-2233

US-GUIDED FOCUSED ULTRASOUND ABLATION

• 22 patients with T1 or T2 breast cancer
  – USgFUSA with no excision
    » Radiation therapy
  – Treatment time = 132 min
  – Followed with Mammo, US, MRI, SPECT

US-GUIDED FOCUSED ULTRASOUND ABLATION

- 55 months f/u
  - 2/22 (9%) local recurrence
  - 94% good to excellent cosmesis

MRI at 18 months

TRANSCUTANEOUS ABLATION OF BREAST CANCER

- Focused Microwave Thermotherapy
- Focused ultrasound ablation
  - ultrasound guidance
  - MRI guidance
MR-G HIFU ABLATION OF BREAST CANCER

• Furusawa, 2006
  – 30 pts, tumor < 3cm
  – distance to skin surface > 1cm
  – IV sedation and analgesia
  – excision 5 to 23 days post-ablation

MR-G HIFU ABLATION OF BREAST CANCER, PATHOLOGY

Red zone: Edema, Inflammation
Thermal coagulation
MR-G HIFU ABLATION OF BREAST CANCER, RESULTS

• Results
  – Two protocol violations resulted in 28/30 for analysis
  – mean of 97% necrosis of targeted tumor volume
  – 3/28 had less than 95% necrosis
  – complications
    » 1 (3%) severe skin burn – Grade 3

MR-G HIFU ABLATION OF BREAST CANCER, NO EXCISION STUDY

• MR-G HIFU ablation under sedation, followed by whole breast RT
  – Inclusion criteria
    » tumor size ≤ 1.5cm
    » well demarcated on MRI
    » definitive diagnosis by core bx.
    » negative nodal status
    » skin-tumor distance ≥ 1.0 cm
MR-G HIFU ABLATION OF BREAST CANCER, NO EXCISION STUDY

• MR-G HIFU ablation
  – post-Tx core needle biopsy under US guidance within 3 weeks of tx.
  – no viable tumor identified in the specimen
  – radiotherapy
  – follow-up MRI q 3-6 months

MR-G HIFU ABLATION OF BREAST CANCER, NO EXCISION STUDY

• Results
  – 74 pts, 1.1 cm mean tumor size
  – mean treatment duration: 120 min.
  – mean f/u 77 months
  – no significant adverse events
  – 1 local recurrence (@8 yrs)
    » 48 patients with > 5 yr f/u

Furusawa, personal communication 1/6/16
MR-G HIFU ABLATION OF BREAST CANCER, EXCISIONLESS STUDY, COSMESIS

MR-G HIFU ABLATION OF BREAST CANCER, EXCISIONLESS STUDY, CASE #1, PRE-TREATMENT

Courtesy of Breastopia Namba Hospital, Miyazaki, Japan
MR-G HIFU ABLATION OF BREAST CANCER, EXCISIONLESS STUDY, CASE #1, POST-TREATMENT

Pre-Treatment T1w+c
Post-Treatment T1w+c
18M FU T1w+c
30M FU T1w+c

Courtesy of Breastopia Namba Hospital, Miyazaki, Japan
MR-G HIFU ABLATION OF BREAST CANCER, EXCISIONLESS STUDY

• Open to accrual in Japan

FUSA in the USA

• Breast Cancer
• Benign Breast Tumors
USgFUSA FOR BENIGN TUMORS

• Single arm study, 20 patients at UVA
• Primary Objective
  – To evaluate the feasibility of USgFUSA for treatment of fibroadenoma
    » Tumor response
    » Patient experience of treatment

USgFUSA FOR BENIGN TUMORS

• Primary Endpoints
  – Palpability of lesion at 12 months
  – Patient tolerability and satisfaction
  – Change in tumor volume
• Measurements at 3, 6, 12 months post-treatment
**USgFUSA FOR BENIGN TUMORS**

- **Inclusion Criteria**
  - 18 years or older
  - Non-calcified fibroadenoma
    - palpable on clinical exam
    - ultrasound
    - core biopsy

**INCLUSION CRITERIA**
Echopulse is a computer-driven system comprised of an Electronics Cabinet, an extra-corporal probe mounted on an arm and moved by motors, a cooling unit and an ultrasound imaging transducer manufactured in France by Theraclion.

**USgFUSA PROCEDURE**

- Patient positioned comfortably on a stretcher
- IV Conscious sedation is provided as needed
- Mass is localized and de-gassed local anesthetic is injected around the tumor
USgFUSA PROCEDURE

• Transducer head is positioned to allow optimal imaging of the mass
• Targeting and treatment planning is performed in multiple planes through the mass

HIFU TREATMENT PLANNING
HIFU TREATMENT PLANNING

TREATMENT PLAN
**WHAT HAPPENS DURING THE PROCEDURE?**

- Alternating ablation and cooling cycles.
- Each pulse lasts several seconds, followed by adequate cooling time.
- Pulse power is adjusted to create boiling of the tissue within sonofication zone.
- Treatment progresses until all of the sonofication sites have been treated.

**ULTRASOUND APPEARANCE DURING THE TREATMENT?**

- Boiling of the tissue can be seen real time during the treatment.
- Surrounding edema can also be seen within the breast tissue.
WHAT IS SEEN ON FOLLOW UP?

• Repeat imaging is performed at 3, 6, 9, and 12 months post treatment

• Patients report resolution of symptoms (lesion is no longer palpable) at 3 months

TREATED FIBROADENOMA

69% Reduction in Volume

Time 0: Prior to HIFU (1.53 cc)

Time 3 Months: (0.47 cc)
TREATED FIBROADENOMA

Pre-procedure 22 x 21 x 10 mm
Volume = 2.4 cc

12 m follow up: 13 x 13 x 7 mm
Volume = 0.6 cc

TREATED FIBROADENOMA

Pre-procedure 20 x 18 x 14 mm
Volume = 2.6 cc

12 m follow up: 15 x 11 x 8 mm
Volume = 0.7 cc
PRELIMINARY RESULTS

- 20 patients treated, closed to accrual
- 11 patients remain in follow-up
- No grade 3 Adverse Events
  - no burns
  - no persistent skin changes
  - no persistent pain

- Pain during treatment
  - 9/16 patients
    » mean 17.8 points on 100 point scale
- Cosmesis excellent, unchanged in all pts (Patient and MD)
- Size on palpation and US reduced in most subjects
PRELIMINARY RESULTS

• Patient satisfaction 4.65 on scale of 5.0
• 91% would undergo procedure again
• 100% would recommend to friend or family

PRELIMINARY CONCLUSIONS

• Well tolerated by patients
• Minimal toxicity
• Appears to be effective.
WHAT’S NEXT AT UVA?

• Pivotal USgFUSA for treatment of fibroadenoma
  – Multi-center study
  – n = 100 pts
  – 3 sites in US, 2 in Europe

UVA FUSA-IMMUNOTHERAPY BREAST CANCER STUDY
ABLATIVE THERAPY FOR BREAST TUMORS

- Preliminary results are intriguing
  - Cryoablation
  - Percutaneous microwave ablation
  - Focused ultrasound ablation
    » US targeting
    » MRI targeting

NON-SURGICAL ABLATION IN THE BREAST

- Need more data to address
  - Local failure rates
  - Cosmesis
  - Cost effectiveness
  - Patient satisfaction
- Combination therapies
• Treating tumors in the breast
  – Fibroadenoma
    » Safety
    » Efficacy
  – Breast cancer

• If a non-surgical ablative therapy is found to be equivalent to surgery
• Then it is likely to become the breast cancer treatment of choice
  – patients will demand it
  – Surgeons should provide it
NON-SURGICAL ABLATION INCOMPLETE TREATMENT

• Breast Preservation
  – Holland, 1985
    » 63% of residual dz.
    » 59% in patients with tumors < 2cm
  – Radiation therapy
  – 4-7% local failure

NON-SURGICAL ABLATION INCOMPLETE TREATMENT

• ACOSOG-Z11
  – No ALND for positive sentinel node
  – 27.3% additional positive nodes
### LENGTH OF PROCEDURE

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<tr>
<th>Procedure</th>
<th>Waiting</th>
<th>Pre-op</th>
<th>In-room pre</th>
<th>Surgery</th>
<th>In-room post</th>
<th>Recovery</th>
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<td><strong>FUSA</strong></td>
<td>120 min</td>
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### US vs MRI GUIDED FUSA

<table>
<thead>
<tr>
<th>MRIgFUSA</th>
<th>USgFUSA</th>
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<tbody>
<tr>
<td><strong>Pros</strong></td>
<td><strong>Pros</strong></td>
</tr>
<tr>
<td>– Measure treatment temp in real time</td>
<td>– Small machine</td>
</tr>
<tr>
<td>– Very precise</td>
<td>– Inexpensive</td>
</tr>
<tr>
<td><strong>Cons</strong></td>
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</tr>
<tr>
<td>– Need an MRI machine</td>
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