Ultrasound-guided High Intensity Focused Ultrasound (HIFU) treatment of breast fibroadenoma

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Introduction

• Breast fibroadenoma (FA) is the most common benign lesion affecting women during their reproductive years.

• The tumour is often seen around the age of 30, but it can be detected at all ages.

• FA occurs in approximately 10% of women during their lifetime.

• FA accounts for between 30% and 75% of all breast biopsies, depending on the age of the population being sampled.
Introduction

• As a consequence of breast imaging development, benign epithelial diseases represent a growing percentage of breast pathology diagnoses.

• Recent data show that benign breast surgery decreases the sensitivity of breast cancer screening, probably due to postoperative mammographic changes.
Principles

- Focused ultrasounds are already used in Europe, USA, Canada, Israel and Japan for the treatment of uterine fibroids under MRI guidance.

- Ultrasound-guided High Intensity Focused Ultrasound (HIFU) is an alternative to the surgical treatment.

- HIFU penetrates through soft tissues and causes localized hyperthermia (around 80°C) responsible of irreversible cell damage, protein denaturation and coagulation necrosis, whereas overlying and surrounding tissues are spared.
Objectives

- The **aim** of our study was to establish the feasibility, safety and efficacy of HIFU technique for breast FA under ultrasound guidance.
A mobile unit with:

✓ an articulated arm integrating the **visualization and treatment unit**
✓ a **cooling system**
✓ a **touch screen interface** for procedure planning and follow-up
Treatment device

Treatment head – an integrated visualization and treatment unit

✓ a membrane with a piezo-electric transducer, 3 MHz resonant frequency, focalized for HIFU
✓ an ultrasound transducer of 7.5 to 12 MHz frequency, integrated in the center of the treatment head for a perfect alignment
Treatment procedure

• The patient is positioned in lateral position

• The breast is well immobilized with an immobilization system

• The treatment head is positioned on the breast
Treatment procedure

• The operator outlines the targeted FA in two axes (radial/antiradial) in order to plan the treatment

• Once the planning is completed, the treatment head will automatically move to cover the whole volume to treat

• The treatment consists in consecutive repeated pulses of HIFU to destroy all the targeted tissues

• Treatment duration varies according to the FA size
Treatment procedure

• During all the procedure, the operator keeps control and if necessary can stop the treatment

• Skin integrity is ensured by a cooling system

• At the end, an ultrasound imaging is performed
Clinical study design

• Inclusion criteria:
  ✓ Women older than 18 years, with a diagnosis of breast FA at:
    - Palpation
    - Ultrasound examination
    - Mammography - for patients of 35 y or older (ACR score < 3)
    - Microbiopsy (CNB) with histology
  ✓ FA size ≥ 10 mm
  ✓ Distance skin/focal point ≥ 11 mm
  ✓ Distance rib cage/FA’s posterior edge ≥ 10 mm
Clinical study design

- Exclusion criteria:
  - Pregnant and lactating women
  - Microcalcifications within the lesion at mammogram
  - Calcified FA
  - Personal breast cancer history
  - Breast implant (treated side)
Patients

• 4 sites in Europe
  – Sofia, Paris, Lille, Valenciennes

• 32 patients, mean age of 30.6±10.8y (16-52y)
  – 23 with solitary FA
  – 9 with ≥ 2 FA in one or both breasts
  – 9 pts with previous surgery for breast FA

• All patients have signed an informed consent
Methods

- HIFU treatment
  - as an outpatient procedure
  - under neuroleptanalgesia
  - mean duration of 1h30 (0h30 - 2h30)

- Post treatment follow-up:
  - physical examination at one week
  - ultrasound and Color Doppler examination every month from M1 to M6, M9 and M12
  - ultrasound volume calculation
Results

- 38 FA treated with HIFU, mean volume 3.49 ml (0.4 - 10.4 ml)
  - 1 FA treated – in 28 pts
  - 2 FA treated – in 2 pts
  - 3 FA treated – in 2 pts

- 3 FA have been retreated 6 months after the first HIFU

- 29 FA with follow-up of 2 to 12 months (M)
Results

<table>
<thead>
<tr>
<th>Follow up period (months)</th>
<th>Mean volume reduction (%)</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M2</td>
<td>32.7 ± 17.0 (6.4 - 62.7)</td>
<td>29</td>
</tr>
<tr>
<td>M4</td>
<td>54.0 ± 11.0 (35.2 - 74.9)</td>
<td>16</td>
</tr>
<tr>
<td>M6</td>
<td>60.7 ± 16.0 (39.0 - 85.9)</td>
<td>12</td>
</tr>
<tr>
<td>M9</td>
<td>61.5 ± 10.0 (46.9 - 70.0)</td>
<td>5</td>
</tr>
<tr>
<td>M12</td>
<td>68.5 ± 6.0 (63.9 - 73.0)</td>
<td>2</td>
</tr>
</tbody>
</table>
Results
Results at M2

**VSM-41yo**

- V0: 2.79
- M1: 1.98
- M2: 1.55
- Reduction: 44%

**JDM2 / R 12h30-42yo**

- V0: 2.15
- M1: 1.46
- Reduction: 53%
Results at M4

**NST-18yo**

- M0: 5.26
- M2: 2.46
- M4: 1.70

**Decrease:** -68%

**GDJ1 / R 14h - 24yo**

- M0: 3.43
- M2: 2.96
- M4: 2.67
- M6: 2.50
- M12: 1.90

**Decrease:** -36%
Results at M6

SOJ – 16yo

RJP – 35yo

-83%

-69%
Results at M9

**ZDZ - 23yo**

<table>
<thead>
<tr>
<th>V0</th>
<th>M2</th>
<th>M4</th>
<th>M6</th>
<th>M9</th>
<th>M12</th>
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</thead>
<tbody>
<tr>
<td>1,75</td>
<td>1,42</td>
<td>0,99</td>
<td>0,83</td>
<td>0,68</td>
<td></td>
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-61%

**MOA - 21yo**

<table>
<thead>
<tr>
<th>V0</th>
<th>M2</th>
<th>M4</th>
<th>M6</th>
<th>M9</th>
<th>M12</th>
</tr>
</thead>
<tbody>
<tr>
<td>0,88</td>
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</table>

-69%
Results at M12

**GKS - 22yo**

- V0: 3.90
- M2: 3.14
- M4: 1.69
- M6: 1.39
- M9: 1.41
- M12: 1.0

Change: -64%

**VID - 27yo**

- V0: 1.87
- M2: 1.47
- M4: 0.76
- M6: 0.66
- M9: 0.50
- M12: 0.5

Change: -73%
Results

Patient 27yo, pregnancy one month after HIFU

Volume reduction over time (%)

- Volume reduction of 73% despite pregnancy hormone stimulation
- Breastfeeding was possible without complication
Color Doppler changes

SOJ before HIFU

SOJ M6

DII before HIFU

DII M6
Color Doppler changes

VID before HIFU

VID M12

VSM before HIFU

VSM M2
Results - histology

One patient have been operated 2 months after HIFU

Mesenchymal cell proliferation around elongated glandular structures

Hemorrhagic tissue necrosis of mesenchyma with some residual glandular structures
Tolerance

• **Side effects**
  
  – 61% - increased sensibility of the treated FA connected with the cycle (between D7 and M3)
  
  – 43,5% - FA induration between D7 and M3
  
  – 30,4% - skin edema between D7 and M1
  
  – 13% - skin irritation and erythema between D7 and M1

• **No serious side effects were observed**
Conclusions

• HIFU is a non-invasive and effective treatment method for breast FA

• The procedure is well tolerated by the patients, with mild to moderate transitory side effects

• Preliminary results are encouraging and show that HIFU could be a successive alternative to surgery for benign breast tumors