Evidence Table

Clinical Area: Cryoablation for breast cancer or benign fibroadenomas of the breast
cryoablation of breast fibroadenomas with long-term follow-up.
Kaufman CS, Littrup PJ, Freeman-Gibbs LA et al. Office-based
cryoablation of breast fibroadenomas: 12-month follow-up, J Am Coll
Kaufman CS, Bachman B, Littrup PJ et al. Cryoablation treatment of
benign breast lesions with 12-month follow-up. Am J Surg 2004; 188:
340-348.

Study Type: Case Series-prospective
Study Aim: To evaluate the safety and efficacy of cryoablation as a primary therapy for benign
breast lesions, including breast fibroadenomas.

Outcomes
- **Primary**: Efficacy outcomes not specified in methods section. Reported on tumor volume and
  palpability.
- **Secondary**: Adverse effects, patient satisfaction.

Design
- **Number of subjects**: N=63 patients (n=78 lesions)
- **Description of study population**: Patients were treated at 8 U.S. sites between 2000-2002.
  Median age=34 years (range=13-66). N=52 had 1 lesion treated/ n=10 had 2 lesions treated/
  1 patient had 6 lesions treated.
- **Inclusion criteria**: Benign breast lesions.
- **Exclusion criteria**: Tumors not visible by ultrasound; history of ipsilateral breast cancer;
  other suspicious breast lesions.
- **Consecutive patients?** Not specified.
- **Intervention**: Patients underwent pretreatment large-core needle biopsy procedures. Up to 3
  tumors could be treated in the same patient at a single treatment session. The cyoablation
  procedure consisted of ultrasound-guided placement of a cytoprobe at the center of a lesion.
  Cryoablation was delivered via a tabletop Visica Treatment System and used a freeze-thaw-
  freeze technique. 78% of cases were performed in the office setting with only local
  anesthesia. 22% of the early cases were performed under general anesthesia of conscious
  sedation. A first generation cytoprobe that incorporates air-gap insulation was used in all but
  the last 6 lesions; the latter were treated with a second-generation cytoprobe that had vacuum
  insulation.
- **Source of outcome data**: Clinical examination; self-examination; ultrasound; mammography.
- **Length of follow-up**: 12-months in main study; some patients were followed longer.

Validity
- **Was population homogenous?** All had benign breast lesions, but different types.
- **Potential selection biases**: Reporting only on cases that were treated per protocol.
• *Were intervention/care/follow-up similar in each group?* Appeared to be.

• *Did an objective observer assess outcomes?* Not specified.

• *Completeness of follow-up:* The 2004 Am J Surg article reported overall 12-month findings in 52 patients (9 were excluded due to protocol violations and 5 were lost to follow-up). The 2004 J Am Coll Surg article reported on 12-month follow-up of patients with breast fibroadenomas (originally 57 patients, follow-up data on 47 patients). The 2005 Breast J article reported on the last follow-up (average=2.6 years) in 32 of the 57 patients with breast fibroadenomas.

• *Conclusions regarding validity of methods:* This was a case series, with no control or comparison group. In their primary analysis, the authors included only patients who were treated according to protocol and were followed for at least 12 months. Only 32/57 (56%) of the patients with breast fibroadenomas were included in the long-term follow-up analysis. The study was funded by Sanarus Medical, the manufacturer of the Visico Treatment System.

**Results**

**Efficacy at 12 months**

*All patients (52/63 patients)*

Median residual lesion volume measured by ultrasonographs 11.7% of pretreatment volume

Note: The 9 patients excluded for protocol violations had an average residual volume of 40% at 12 months.

Lesions that were clinically palpable (>1 cm) decreased in number from 71% to 20%.

*Patients with breast fibroadenomas (47/57 patients with this type of lesion)*

*Note: This is a subset of the patients discussed above*

Median residual lesion volume measured by ultrasonographs 11% of pretreatment volume

Of tumors with <2.5cm maximum pretreatment diameter (n=43), 86% were non-palpable at 12 months (did not report how many were non-palpable initially)

Of tumors >2.5 cm maximum pretreatment diameter (n=11), 62% remained palpable at 12 months.

*Breast fibroadenomas at last follow-up (32/57 patients with this type of lesion (mean follow-up 2.6 years))*

Median residual volume measured by ultrasonographs was 99% at the most recent follow-up.

Of tumors ≤2.0 cm maximum pretreatment diameter, 16/17 (94%) were non-palpable at the most recent examination (did not report how many were non-palpable initially)
Of tumors >2.0 cm maximum pretreatment diameter, 11/15 (73%) were nonpalpable at the most recent examination.

Safety

There were no major complications in any of the three articles

**Number of peri-procedural minor complications (only patients with breast fibroadenomas, n=57)**

- Moderate to severe postprocedure pain: 2
- Hematoma (mild): 2
- Mild thermal skin injury: 4

**Note:** All of the above complications were associated with the first generation cytoprobe

**Number of longer-term minor complications (whole group), total no. for safety analysis=63**

<table>
<thead>
<tr>
<th></th>
<th>6 weeks</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local skin depigmentation</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Tape blisters</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Keloid at probe entry</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Breast abscess</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Long-term follow-up in 32 patients**

2 patients who had been lost to follow-up earlier but returned for an examination at 2.7 years reported mild tenderness in the treated area. Another patient reported cyclical focal pain in the area—that pain had also not been reported at 1 year.

**Authors’ Conclusions**

(Am J Surg 2004) “Ultrasound-guided cryoablation is an effective and safe treatment for benign breast lesions, as seen at 12-month follow-up and offers an office-based, minimally invasive alternative to surgical excision.”

**Reviewer’s Conclusions**

Most of the breast lesions, particularly the smaller lesions, dramatically reduced in size after cryoablation and there were no major complications. Study limitations include that findings were not reported for all the original patients in the case series, there was no comparison to any other treatments or conservative management and the study was funded by the manufacturer of the cryoablation system.

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