

**Surgical tools
for improved intra-operative
excision margin assessment
in breast-conserving surgery**

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December 11, 2007

Terminology

Breast-Conserving Surgery (BCS)

Surgical removal of a breast tumor with a *safe margin* of normal tissue

usually supplemented with radiation therapy to control residual microscopic disease (then called Breast-Conserving Therapy, or BCT)

“superior”
orientation
marker

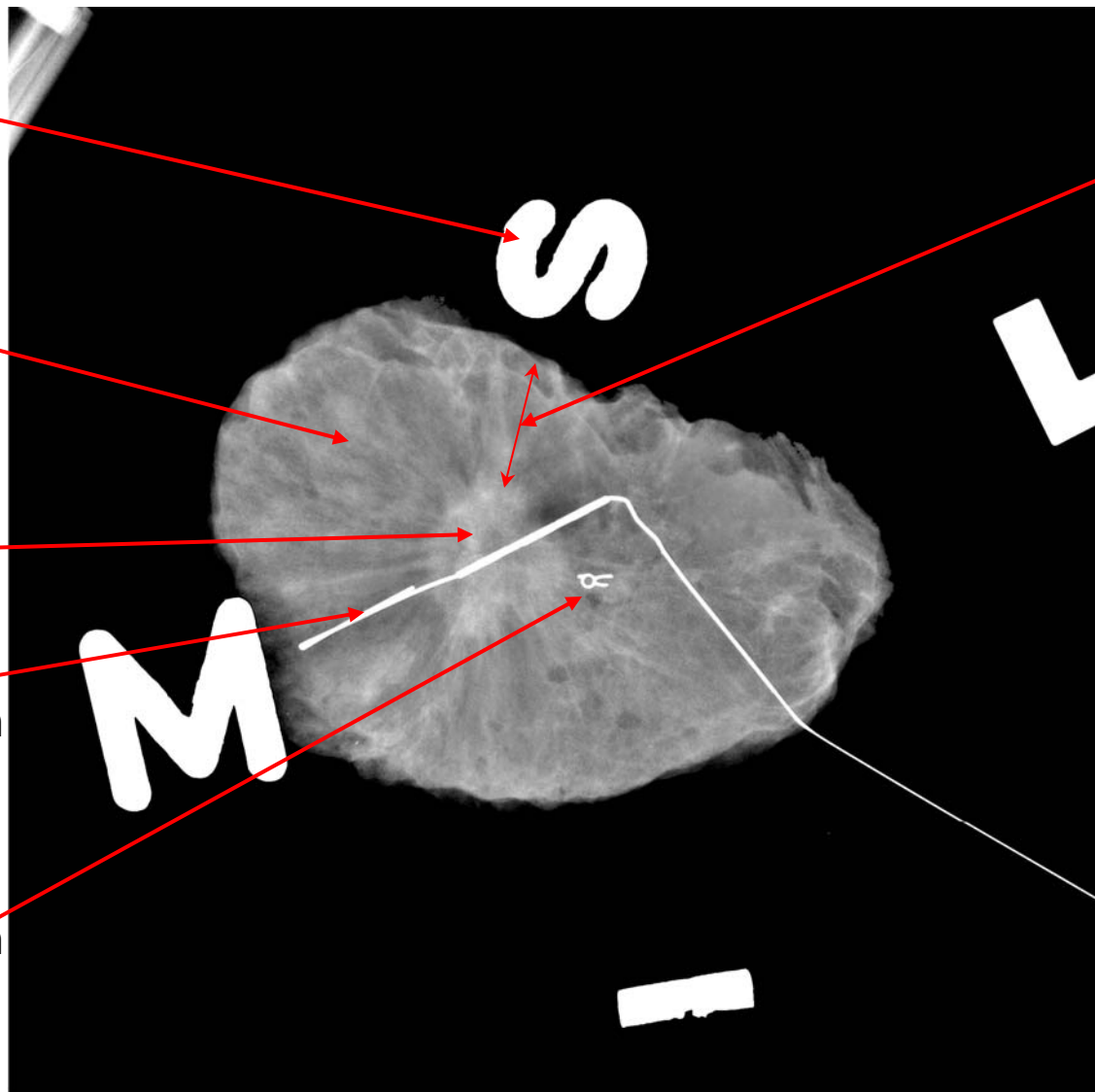
radiographic
margin

specimen

tumor

Localization
wire

Localization
clip



A 25 year study by the National Surgical Adjuvant Breast and Bowel Project (NSABP) showed that there was **no significant difference in survival** between women treated with **radical mastectomy** and those treated with **BCT**

Fischer et. al., Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer.

N. Engl. J. Med. Volume 347(16). 2002. 1233-1241.

Background

Of the **210,000** women diagnosed with breast cancer each year **in the U.S.**, and an additional **360,000 in the E. U.**, more than **half** will opt for breast conserving therapy, rather than mastectomy, despite a five-fold **increase in the risk of local recurrence.**

Goldfeder S., Davis, D., Cullinan, J. Breast Specimen Radiography: Can It Predict Margin Status of Excised Breast Carcinoma

Acad Radiol 2006; 13:1453-1459

Ferlay, J., Bray F. Pisani P., Parkin, D.M. Globocan 2002, Cancer Incidence, Mortality and Prevalance Worldwide. IARC CancerBase No. 5, Version 2.0. IARCPress, Lyon, 2004

Background

Residual breast cancer detected at the margins of excised breast specimens indicate a local breast cancer recurrence rate of over 16%, as compared with 3% when negative, or clear, margins are obtained.

Smitt, MC., Nowels, K, Carlson, R., Jeffrey, S. Predictors of re-excision findings and recurrence after breast conservation

Int. J. Radiation Oncology Biol. Phys. Vol. 57, No. 4, pp. 979-985, 2003

Background

Fundamental clinical challenge in breast-conserving therapy is the **balance between risk of local recurrence and cosmesis.**

Background

Primary excision yields histologically positive margins 20% to 55% of the time, requiring a re-excision!

Klimberg VS., Harms S., Korourian S. Assessing margin status. Surg. Oncol. 1999; 8:77-84.

Clinical Challenge

Definitive permanent section histopathology of excised specimen margins is not available until well after the patient leaves the O.R.

(intraoperative frozen section and touch prep analysis are not widely used due to technical and clinical limitations.)

LONG-TERM OBJECTIVES

For patients selecting breast-conserving surgery over mastectomy:

- 1. Reduce local recurrence of breast cancer.**
- 2. Reduce surgical re-excision rates.**

For surgeons performing breast-conserving surgery:

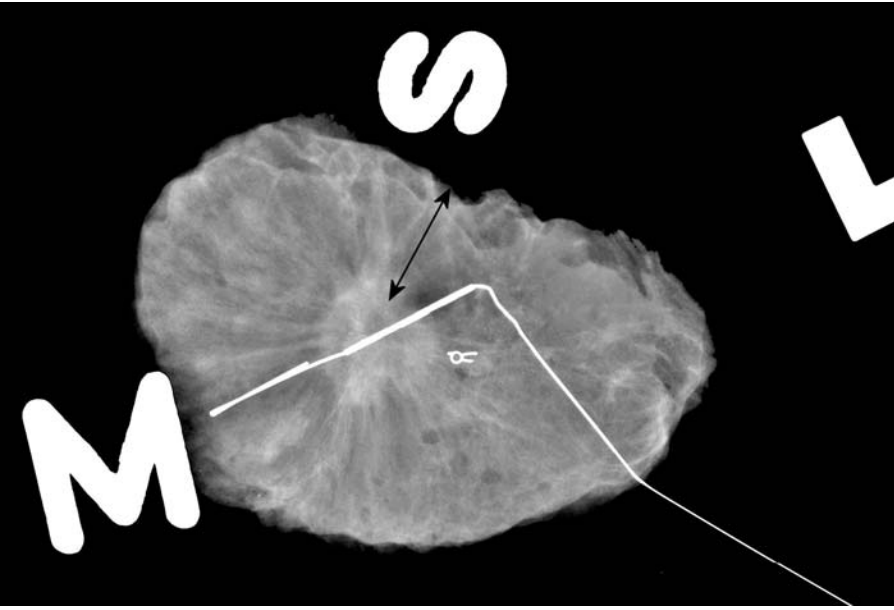
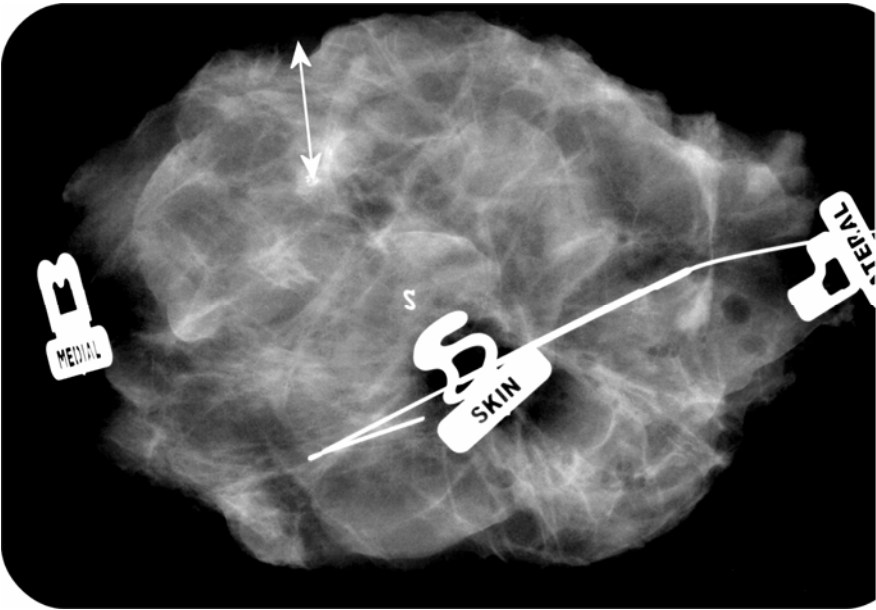
- 1. Reduce operating procedure time**
- 2. Simplify clinical communications between the O.R. and radiology and pathology departments**

Initial Implementation

We propose a new disposable tool to improve the concordance between intraoperative radiographic margin assessment and gold-standard permanent section histopathology of margins in breast conserving therapy.

Improvements in **intraoperative radiographic assessment of margins** –

Bioptics Digital Specimen Radiography System





Bioptics
Digital Specimen Radiography System

FDA 510(k) cleared in Oct. 05

Portable unit; rolled in to the O.R.

**Auto kV and exposure time;
one-button operation**

10 seconds from x-rays to display

10 lp/mm (contact); 14 lp/mm (x1.4 mag)

**DICOM image transmission to
Radiology and Pathology**

Historical specimen radiography methods provide limited intraoperative margin assessment value...

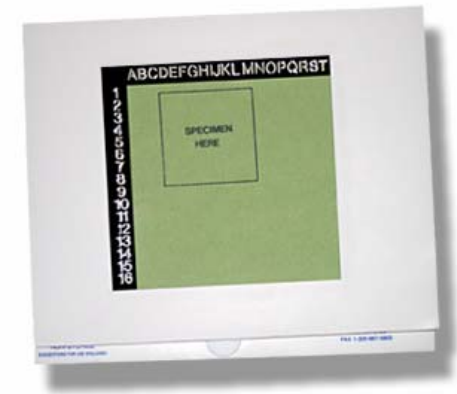
Sensitivity of specimen radiography = 55% - 62%

Specificity of specimen radiography = 88% - 95%

“Analysis of the use of specimen mammography in breast conservation therapy”
McCormick et al. The American Journal of Surgery 188(2004) 433-436
“The Efficacy of Specimen Radiography in Evaluating the Surgical Margins of
Impalpable Breast Carcinoma” Graham et. al. AJR 1994; 162:33-36

...partly due to the **limitations of disposable tools** used in intraoperative radiographic margin assessment

- Typically two pieces of cardboard, within which the specimen is placed and compressed
- X-ray images acquired with specimen inside the container
- Specimen transported to Pathology inside the container



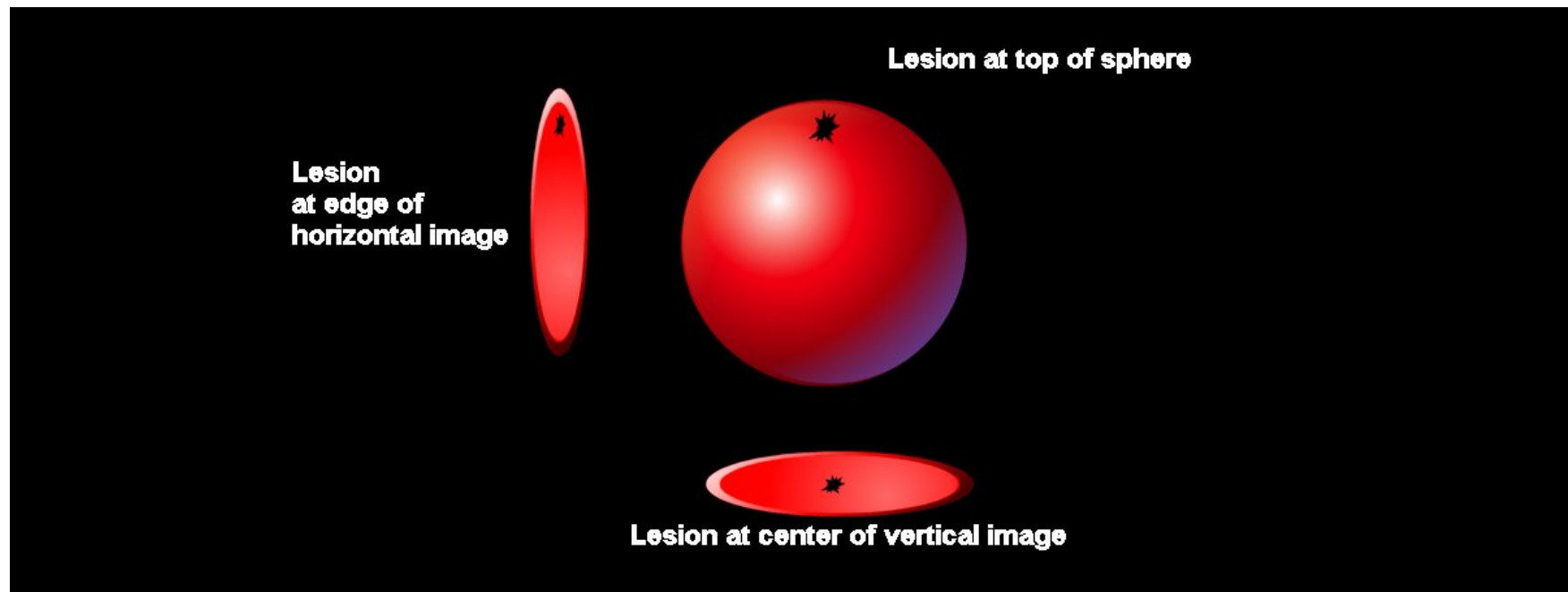
Technical limitations of current disposable tools

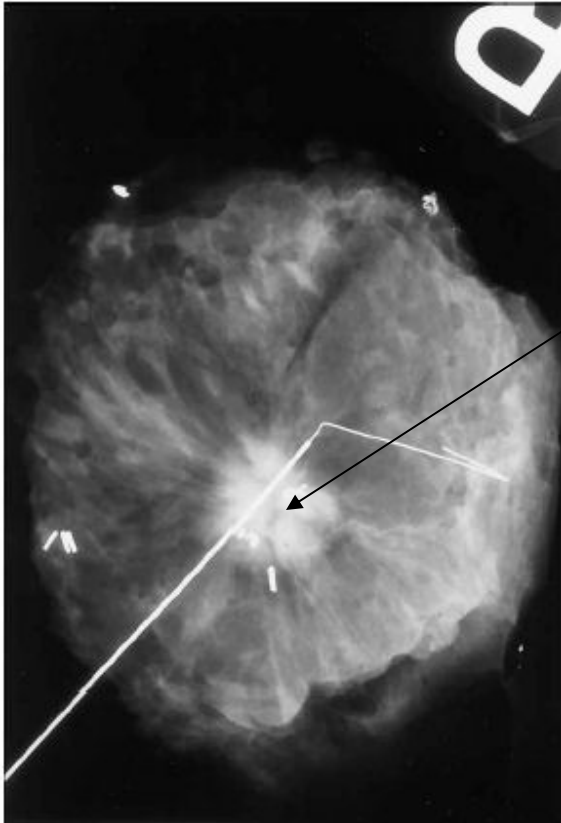
- #1 Commercially available specimen container devices do not permit convenient **orthogonal imaging** of specimens, resulting in possible **misinterpretation of margins in up to 7% of cases.**

Rebner, M., Pennes, D., Baker, E., Adler, D., Boyd, P. Two-View Specimen Radiography in Surgical Biopsy of Nonpalpable Breast Masses

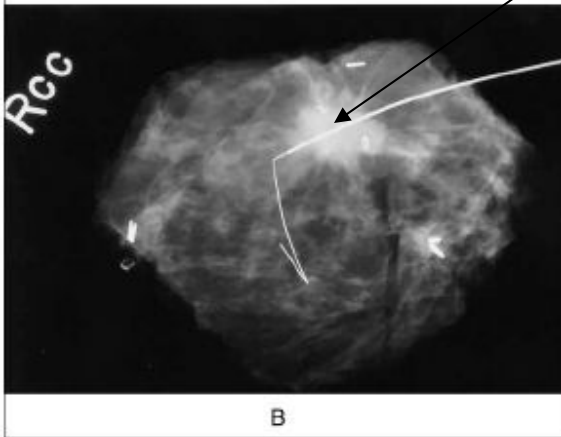
AJR 149:283-285, August 1987

Improved Margin Assessment by Orthogonal Imaging





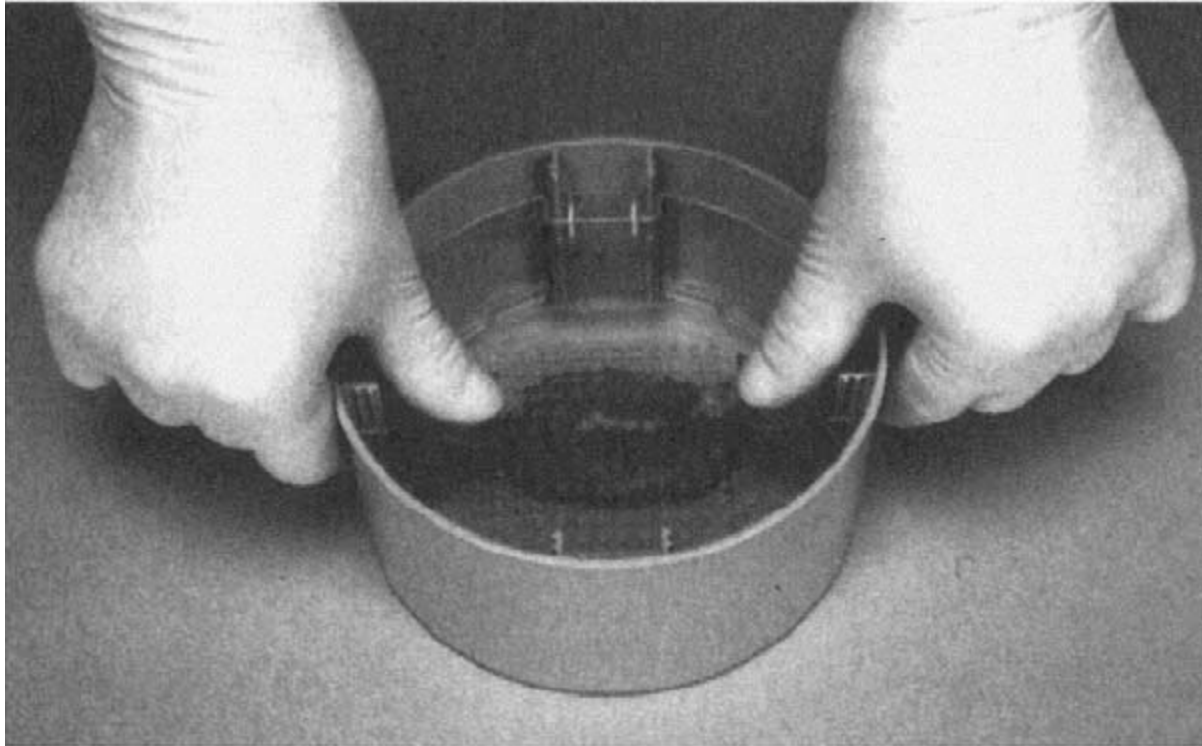
Tumor at center of specimen
In vertical view

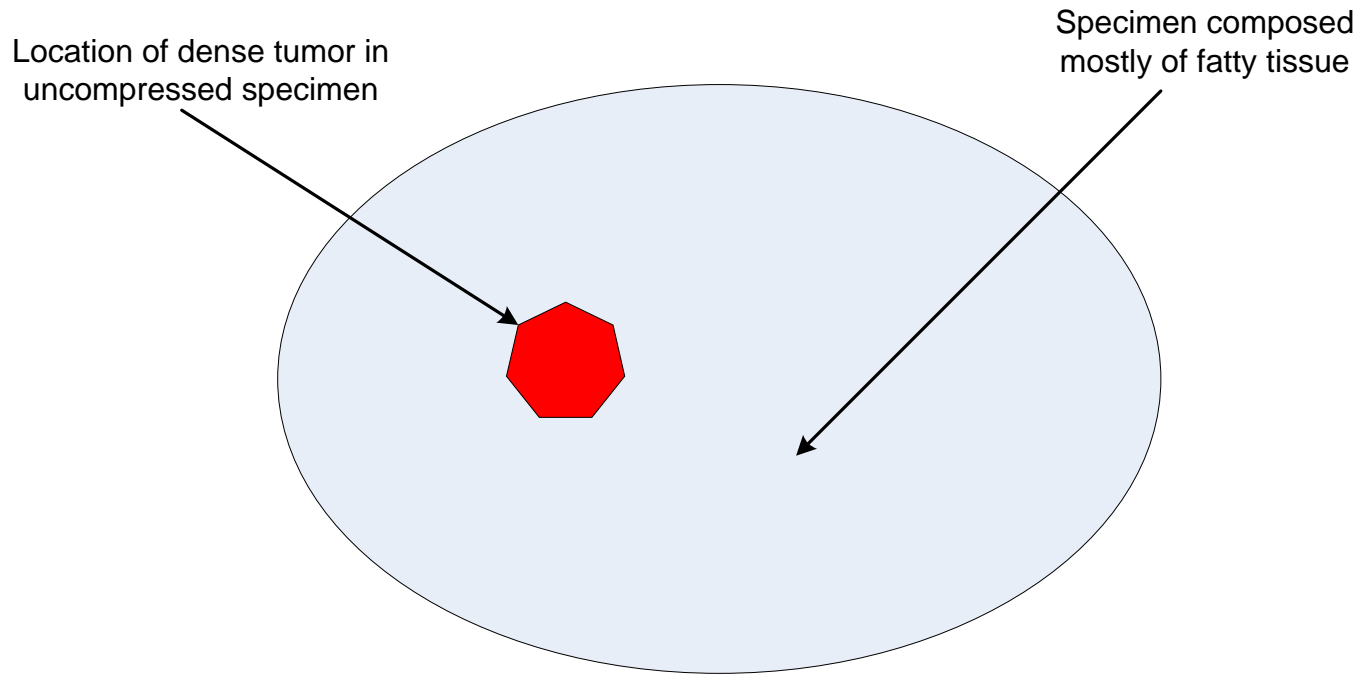


Tumor at specimen edge
In horizontal view

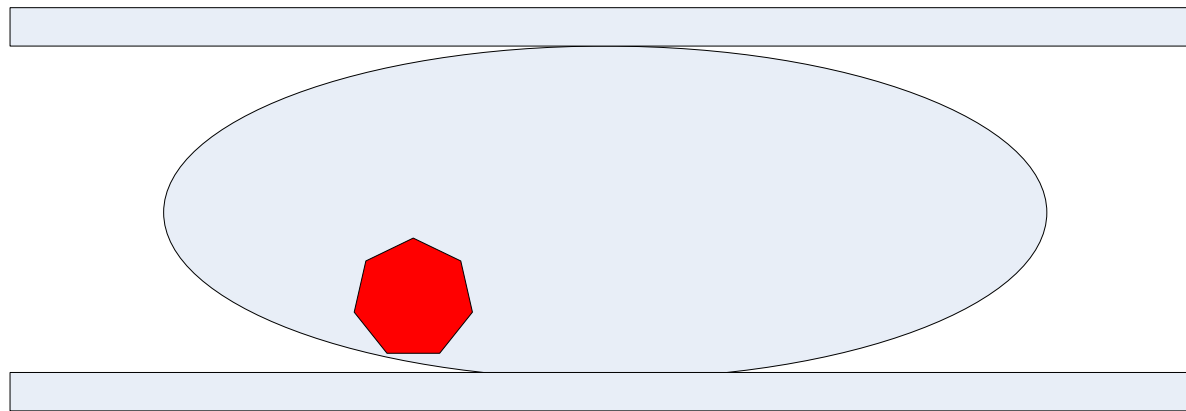
At Temple University, where these images were taken, two-view radiography **reduced re-excision rates from 12% to 5%²⁶**.

TranSpec Specimen Radiography Device by E-Z EM Corp.





Clear margins in uncompressed tissue



False positive margin caused by excessive compression due to the “pancaking” effect

Current technical limitations

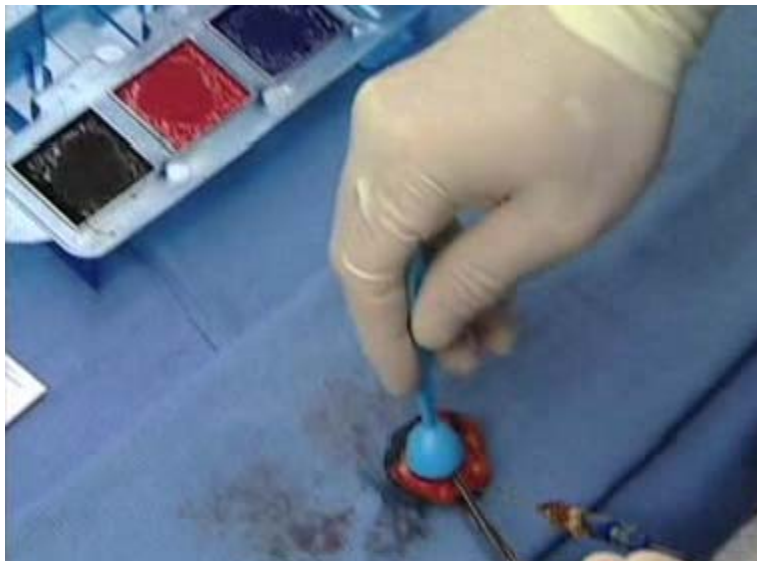
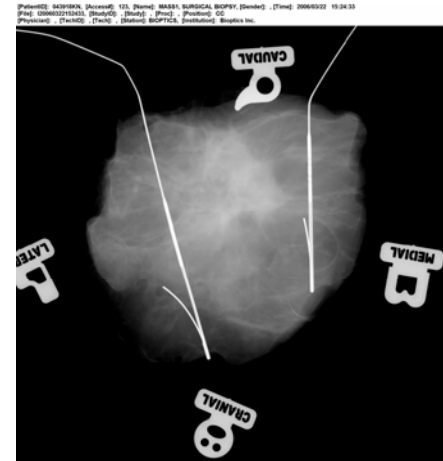
- #2 Commercially available specimen container devices can result in **excessive tissue compression**, leading to **false-positive margins** due to the displacement of the tumor under compression, which may account for up to **63% of unnecessary re-excision lumpectomies**.

Dooley, WC., Parker, JP. Understanding the mechanisms creating false positive lumpectomy margins
American Journal of Surgery 190 (2005) 606-608

Current technical limitations

- #3 Commercially available specimen containers do not contain complete **three dimensional spatial localization information**, requiring the use of precious O.R. time with surgical sutures, and differential inking

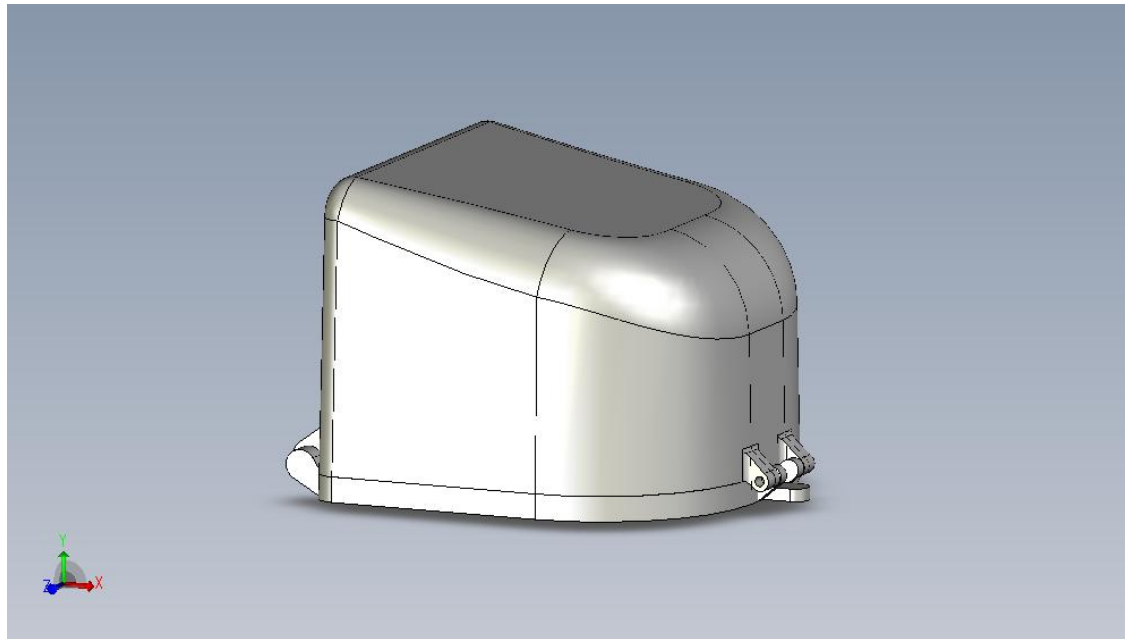
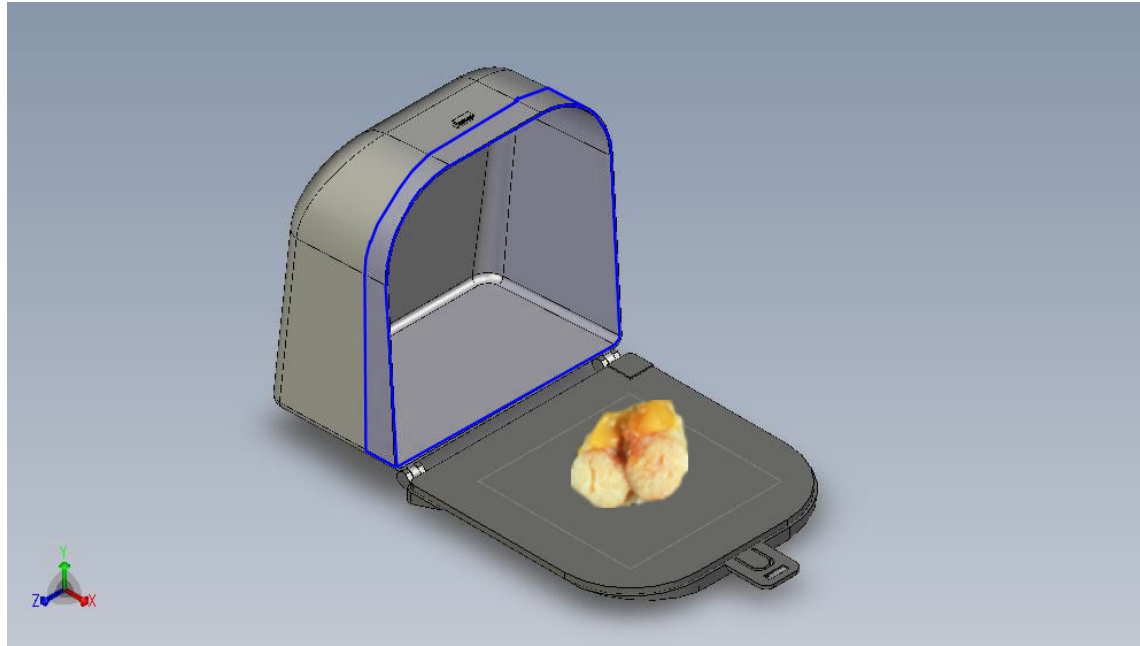
Use of surgical sutures and ink in the O.R. for specimen orientation

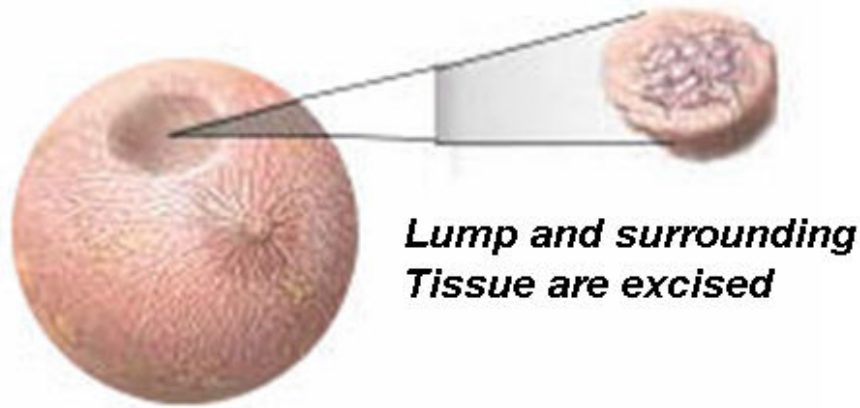


Proposed Solution

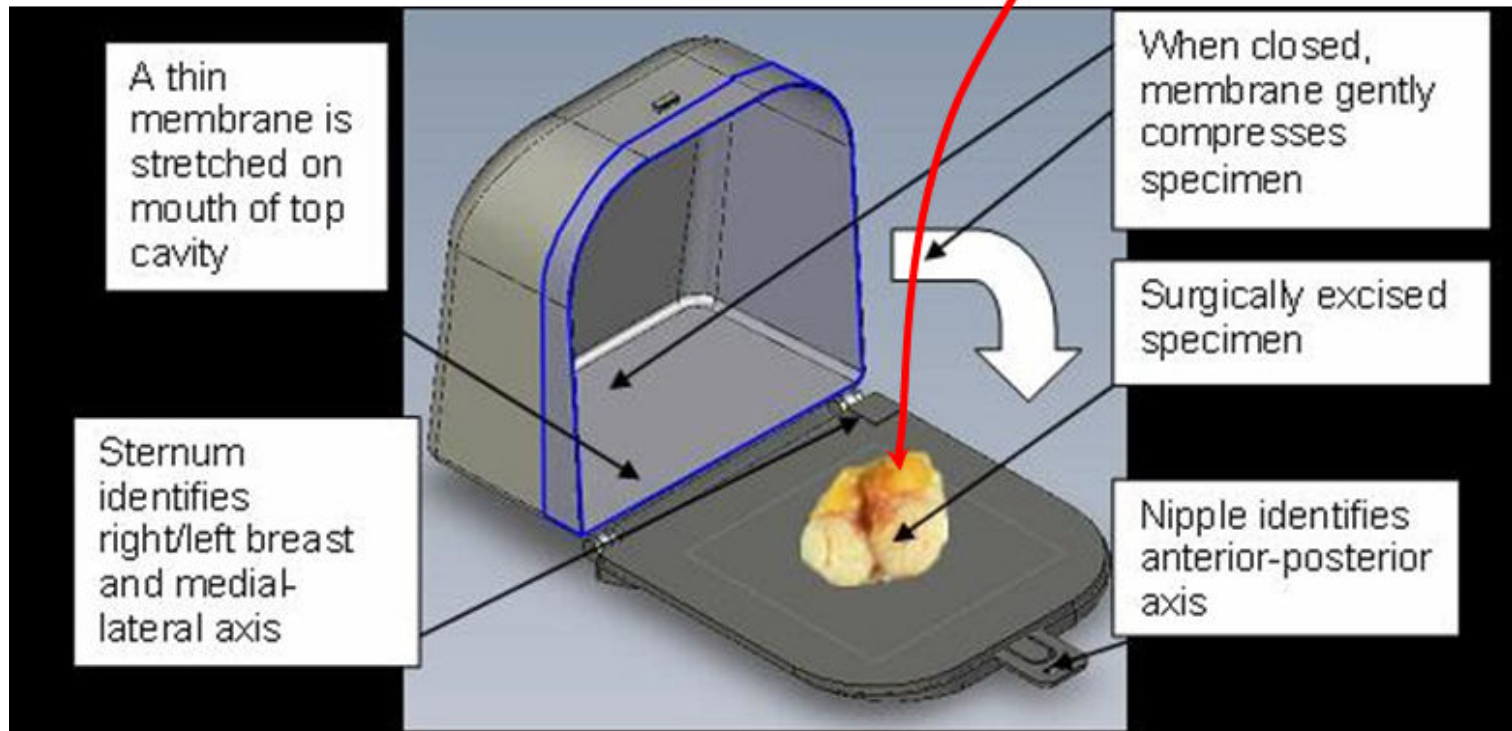
A novel “breast-shaped,” clam-shell specimen container, which provides:

1. Convenient two-view radiography
(cut re-excision rates in half at Temple Univ.)
2. Gentle compression of specimen
(eliminated 63% of false positives)
3. Three dimensional orientation information, obviating the need for surgical sutures, and differential inking by surgeon in the O.R.
(15 min O.R. time savings per procedure)

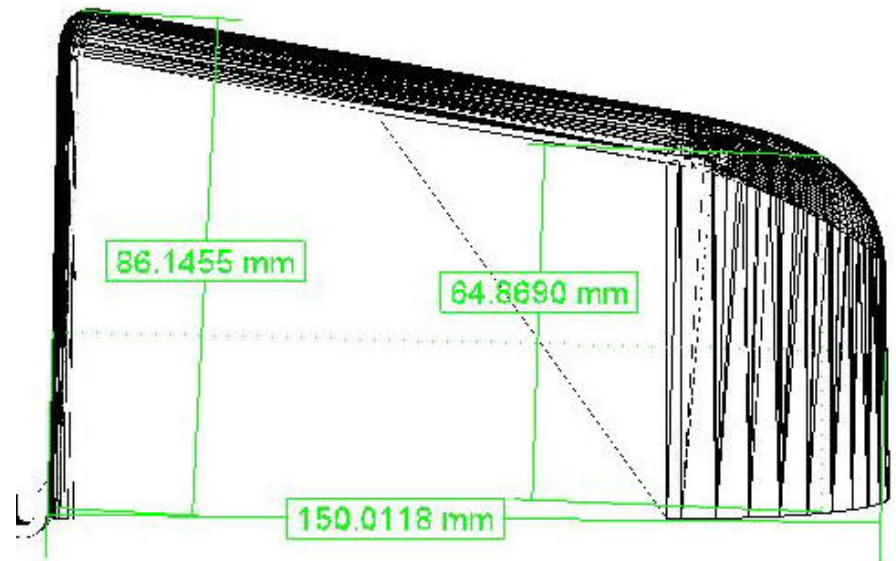
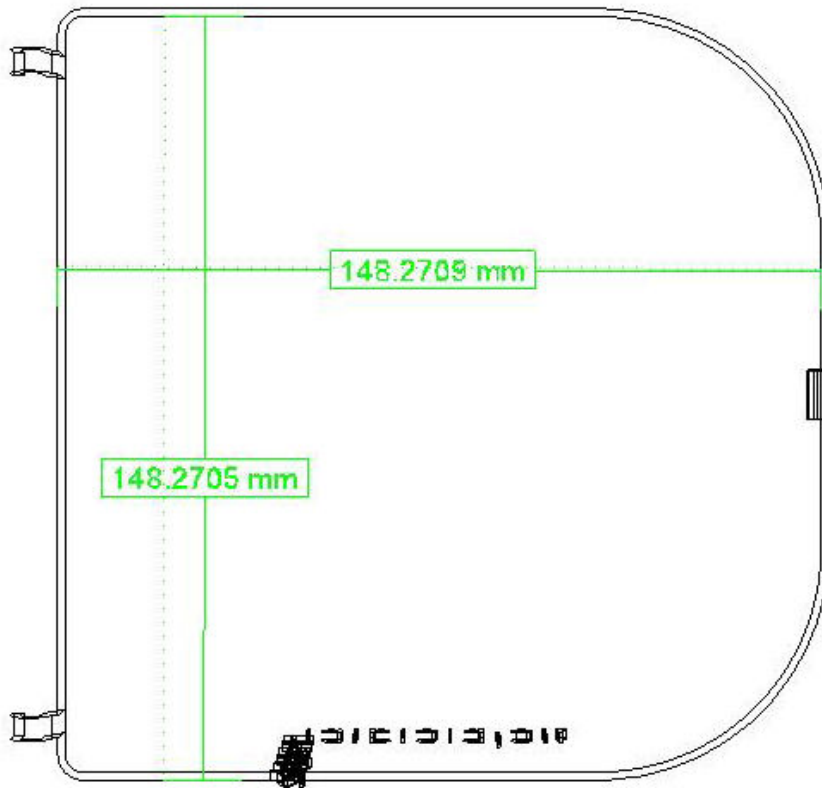




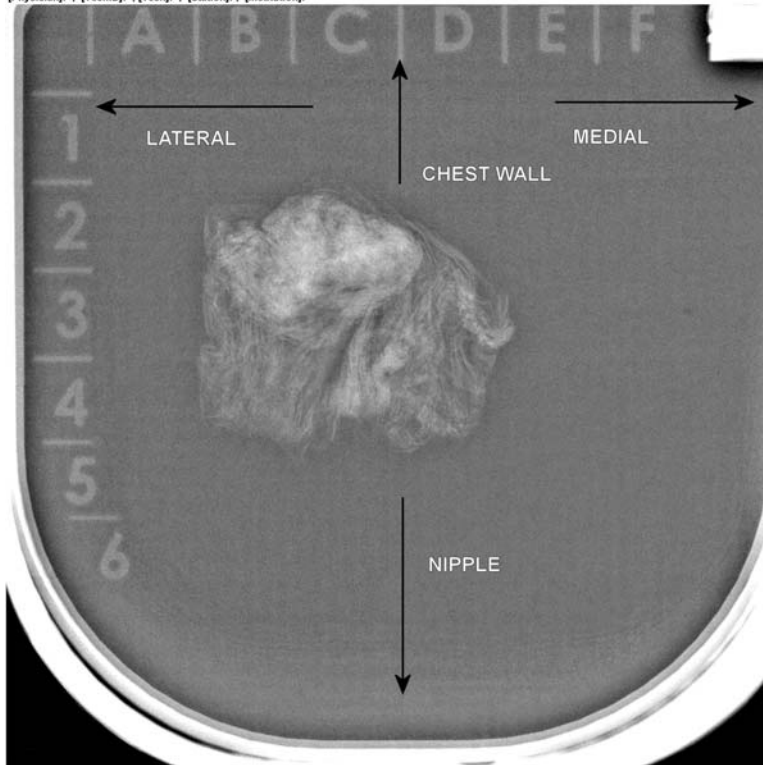
and placed in container in the same 3-D orientation



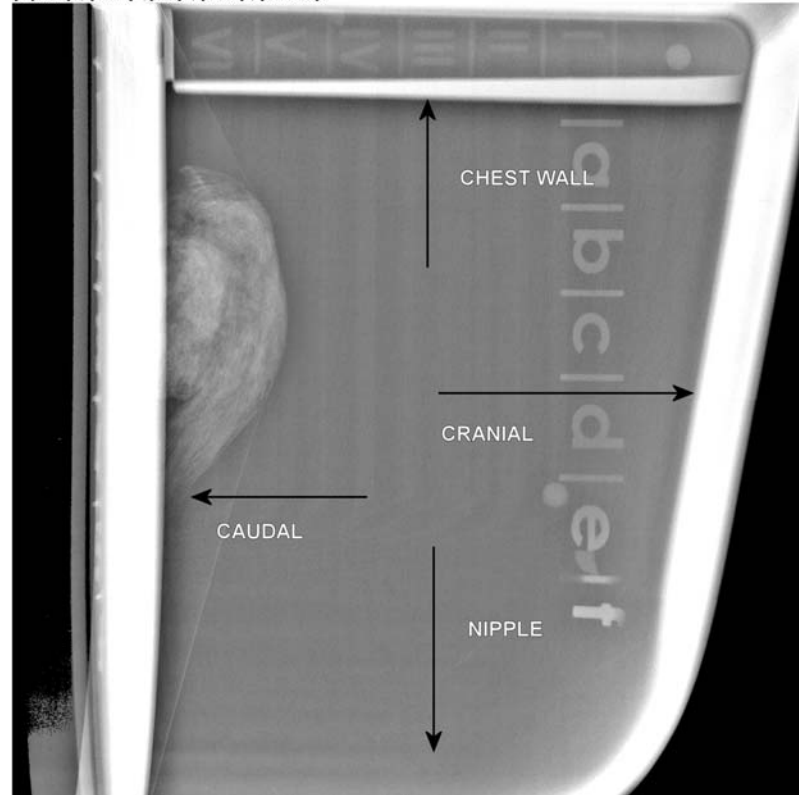
Mechanical dimensions



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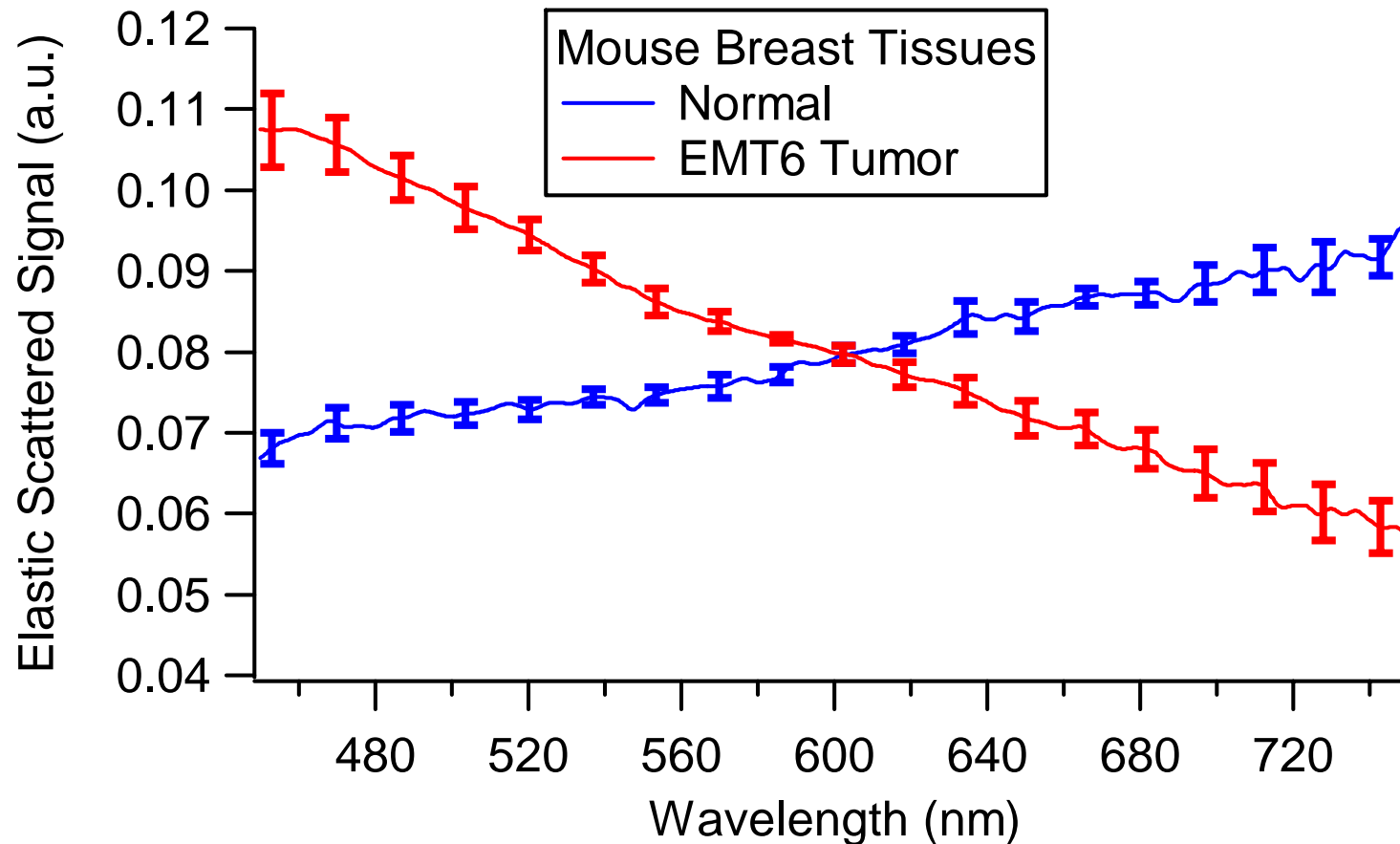


Orthogonal views of specimen in the specimen container box showing gentle compression of specimen and fiducial markers

The container enables
a novel secondary product to
further reduce re-excision and
local recurrence rates in BCS

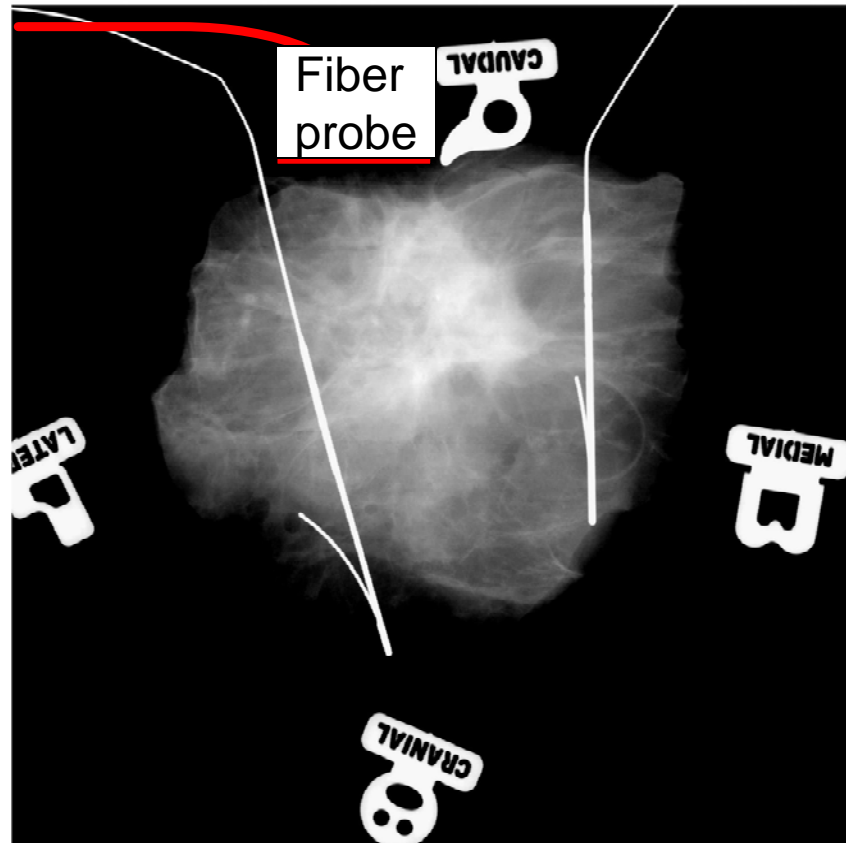
- Two-view intraoperative digital specimen radiography, utilizing a novel specimen container
- **Ex-vivo margin assessment utilizing intraoperative orthogonal digital x-ray imaging guided optical spectroscopy**

Elastic Light Scatter Spectroscopy



M. Canpolat, J. R. Mourant Canpolat, "Particle Size Analysis of Turbid Media Using a Single Optical Fiber in Contact with the Medium to Deliver and Detect White Light", Applied Optics Vol. 40, No: 22, pp 3792-3799 , 2001.

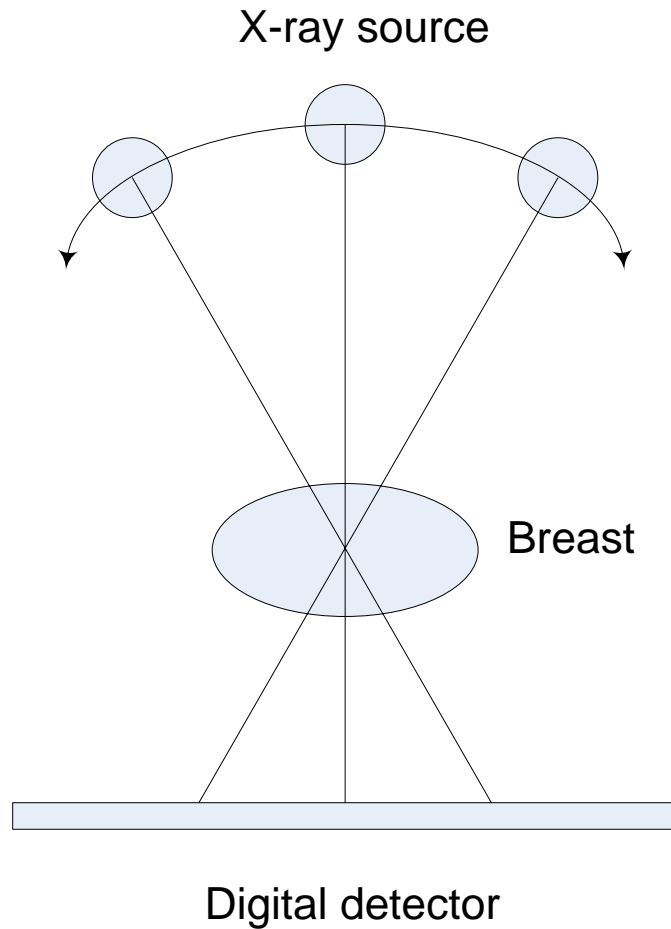
Orthogonal digital x-ray imaging guided margin assessment by optical spectroscopy



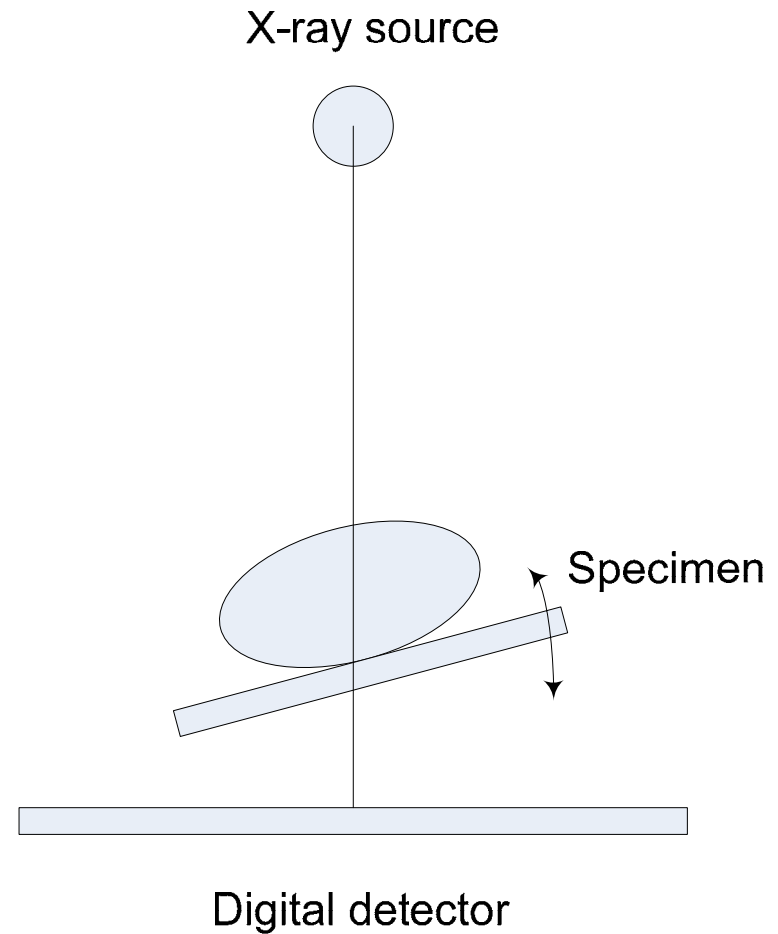
Excision margin assessment
by optical spectroscopy in BCS
is an optimal clinical test-bed
for the application of the
principle of spectroscopy
to other forms of cancer
(cervical, brain, skin, etc.)

The container enables
a novel third product to further
reduce re-excision and local
recurrence rates in BCS

Margin assessment by 3-D tomosynthesis



Breast tomosynthesis geometry

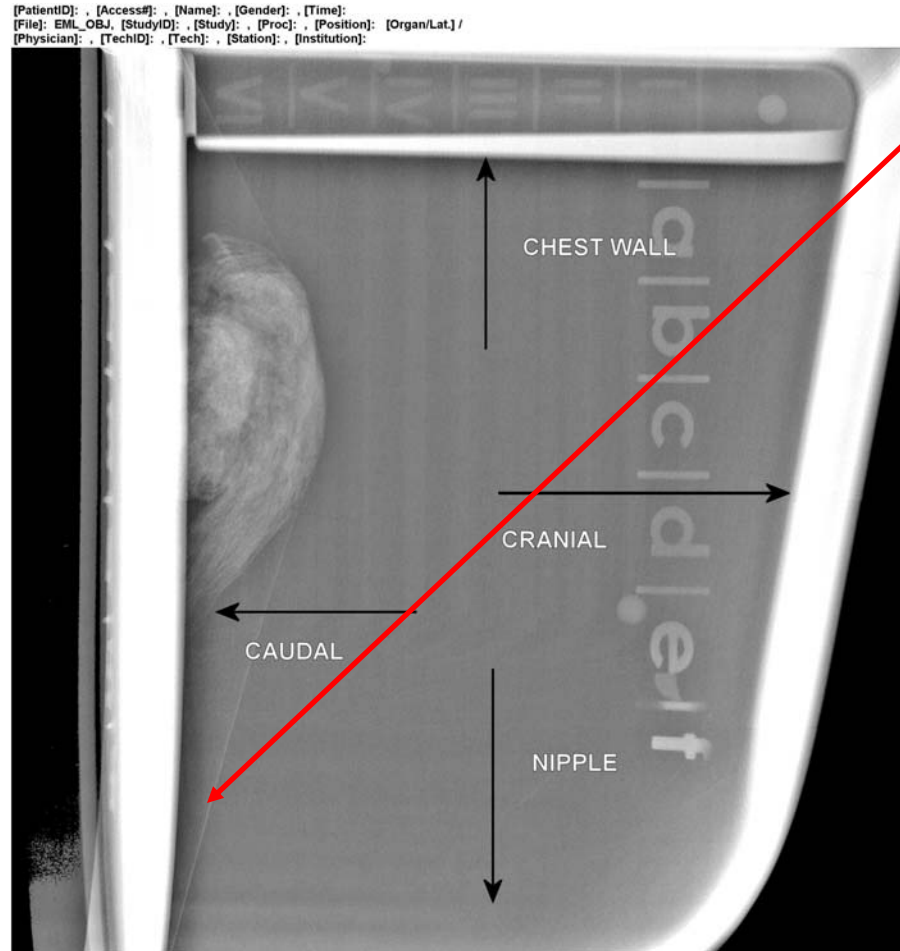


Specimen tomosynthesis geometry

Challenges associated with specimen tomosynthesis:

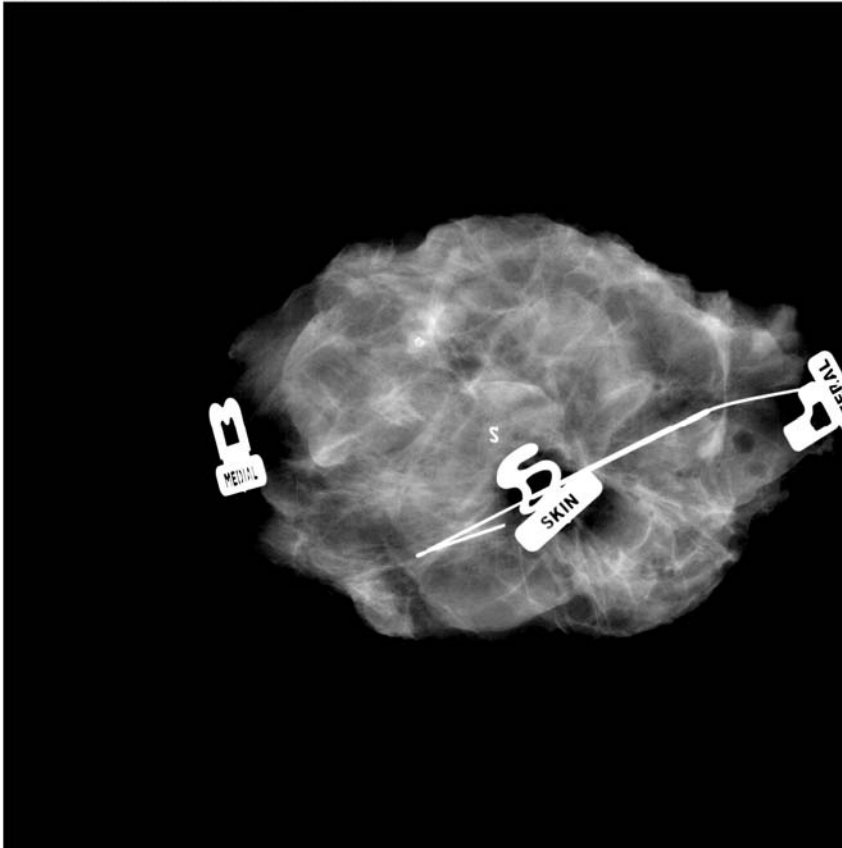
1. Motion artifacts
2. Artifacts arising from metal surgical sutures in the specimen

Motion artifacts – specimen immobilized by membrane

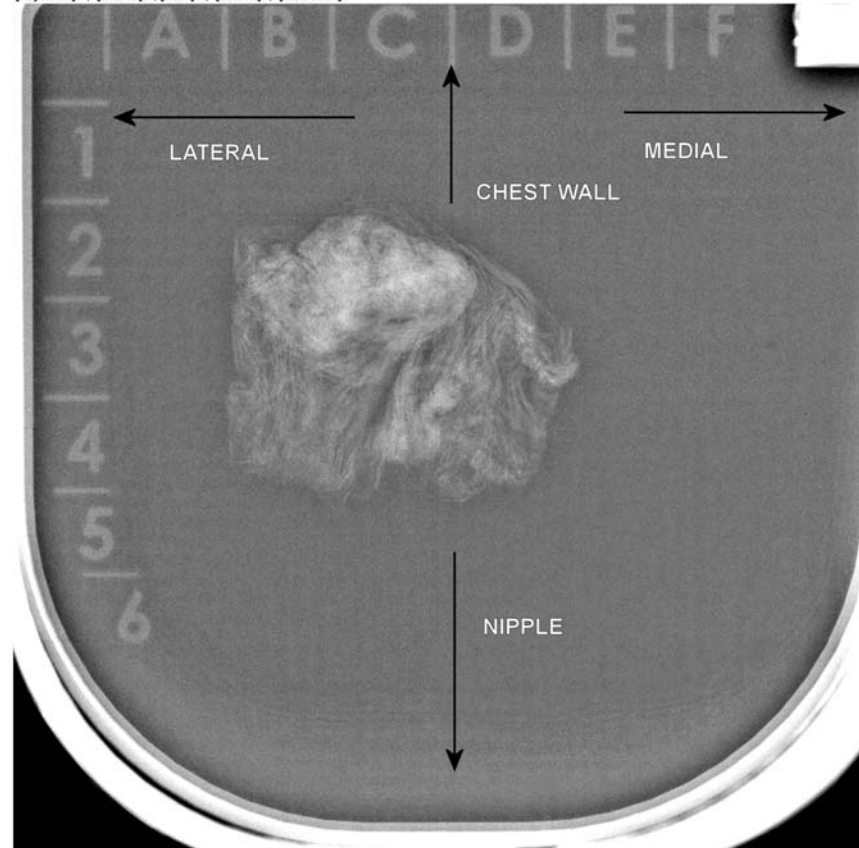


No sutures => no suture artifacts

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Excision margin assessment
by specimen tomosynthesis in BCS
is an optimal clinical test-bed
for the application of the
principle of tomosynthesis
to full-field digital mammography

Thank You