

Reflections

3-D automated ultrasound (ABUS)

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INTRODUCTION

The 3D image of the four basic building blocks in the breast







The normal breast contains 12-15 lobes, each composed of a main duct and its branches (as in a tree), terminating in the lobules (like leaves on a tree), all surrounded by supporting fibrous or fatty connective tissue.

3D histology of the basic building blocks



12-18 lobes



Cooper was the pioneering researcher of breast anatomy, who published (in 1840 !) the classic work, *On the Anatomy of the Breast.*





The *four "building blocks"* of the normal fibroglandular tissue can be well demonstrated individually on the mammogram/breast ultrasound/MRI of the breast:

Terminal ductal lobular unit (TDLUs)
Ducts and their branches
Fibrous tissue (collagen)
Adipose tissue



Together, they form a harmonious pattern that will be changed by any kind of pathologic lesion, benign or malignant.

The *four "building blocks"* of the normal fibroglandular tissue can be well demonstrated individually on the mammogram/breast ultrasound/MRI of the breast:





Terminal ductal lobular unit (TDLUs).



Building block # 1: Terminal Ductal Lobular Units (nodular densities on the mammogram/3D ultrasound).





The modern breast imaging methods, mammography, breast MRI, automated and hand-held ultrasound, are able to demonstrate the normal ducts and lobules, so that the pathologic lesions developing from these

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structures can be detected early on in their development.

The nodular densities (white dots), corresponding to the lobules, dominate the mammographic image in this case. The gray fatty tissue surrounds the individual lobules, making it possible to distinguish them from each other.







The TDLUs are larger, which is reflected on the mammograms as larger nodular densities.

Atrophic TDLUs (tiny nodular densities) and ducts (thin linear densities) are still visible in the upper portion of the breasts.



With declining hormonal influence, the TDLUs begin to atrophy while the fluid they produced remains in the duct system.



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Automated Breast UltraSound (ABUS)

The automated breast ultrasound (ABUS) examination produces consecutive, 2 mm thick image slices from the skin to the chest wall.



A breast cancer or a fluid-filled cyst cause defects in the normal breast structure, enabling the detection of small lesions that might be hidden on the mammogram.



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MRI exam courtesy: Bruce Porter, M.D., Seattle







Each of these breast imaging methods has its own strengths and weaknesses, which is why evaluation of breast lesions usually calls for their use in combination.



The lobule and the terminal duct, which drains it, form an integrated functional entity, called the terminal ductal lobular unit (TDLU)



Most benign and malignant breast diseases originate from the TDLU, not from the ducts.

The *four "building blocks"* of the normal breast tissue can be well demonstrated individually on the mammogram/breast ultrasound/MRI of the breast:



Building block # 2: Adipose tissue





Complete atrophy of the TDLUs with an increase in the amount of fatty connective tissue.



Normal skin of the breast and the fatty connective tissue beneath it.









Most malignant breast diseases originate from the TDLU, not from the ducts.







A 6 mm spiculated breast cancer (appearance similar to a sea urchin) arising in the TDLU is shown on mammographic images, on an automated ultrasound image in the coronal projection and on a thick section (3D) histologic image.

The *four "building blocks"* of the normal breast tissue can be well demonstrated individually on the mammogram/breast ultrasound/MRI of the breast:



Ducts and their branches





Building block # 3: ducts and their branches (linear densities on the mammogram).







The major ducts converge on the nipple.



When not distended, the normal ducts are pleated and are about 0.1 mm in diameter.





The pleats follow the twists in the major ducts.

The pleats will disappear when the duct is distended by accumulating fluid or cancer cells.



Over time, as the protein-rich fluid accumulates and distends the ducts and their branches, the pleats will disappear entirely and the fluid becomes concentrated (yellow on the image).







The highly proteinaceous, concentrated fluid may calcify and outline the ducts and their branches (secretory "disease" type calcifications).

One type of breast cancer that develops in the larger ducts may produce long, irregular, branching calcifications, which are easily seen on the mammograms.

Ducts distended by tumor cells, debris and amorphous calcifications.







Mammographic-histologic correlation of ducts distended by tumor cells, debris and calcifications.







MRI of the breast: Corresponding to the malignant type calcifications found at mammography, MRI demonstrates malignant breast disease covering a region measuring 11x5x3 cm


The *four "building blocks"* of the normal breast tissue can be well demonstrated individually on the mammogram/breast ultrasound/MRI of the breast:





Fibrous tissue (collagen)

Building block # 4: Collagen (connective tissue)





Collagen (connective tissue)





Fibrous tissue









Classification of normal breast anatomy into structural groups using large section / subgross / mammographic correlation

will simplify the decision process required to differentiate normal from abnormal.

The breast, unlike any other organ, has five structurally different parenchymal patterns



Low risk group

High risk group

These patterns can affect the detectibility of small breast cancers

JAMA Jan 1982.







The issue of "imaging dense breasts": Mammographic parenchymal patterns: I, IV and V.



In women with Patterns I, IV, V the success of finding breast cancer early enough using *mammography only* may be considerably jeopardized.

Background

 Mammography can detect breast cancer at an earlier stage in its development, and it is highly sensitive (80-85%) in asymptomatic women.

• The sensitivity of mammography is limited in women with dense breast, as low as 50%.



Background

 Increased breast density is a major limitation to the effectiveness of mammography in cancer detection among those women attending screening.



Frequency of women with dense breasts

- Two-thirds of premenopausal women
- 25% of all perimenopausal women



Kolb, T et al



Frequency of women with adipose breasts by age



Tabar L, T Tot & PB Dean The Art and Science of Early Detection with Mammography, Thieme Verlag

Background

Hand-held ultrasound examination of the breast has broad acceptance among radiologists in diagnostic evaluation of

- Palpable lesions and
- Screen detected abnormalities

Hand-held ultrasound units are specifically designed and manufactured for

assisting in differential diagnosis



Background

The main limitations of hand-held ultrasound:

Operator dependent / operator variation and
Poor standardization of the technique



Background

There is an urgent need for an automated ultrasound unit that has been specifically designed and manufactured for screening purposes *and* helps reduce the limitations of the hand-held technique



A Promising Solution Specifically Designed for Imaging Dense Breast Tissue

by László Tabár M.D., F.A.C.R. (Hon.)

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Automated 3-D ultrasound screening

INTRODUCTION

Correlation of subgross, thick section (3-D) histologic images of normal and pathologic breast tissue with reconstructed coronal 3D automated ultrasound image slices.





Skin level



ABUS image of the skin and the nipple-areola complex



Anatomic specimen: Low kV mammographic image of the skin after removal of the glandular tissue.





The nipple-areola complex gives a characteristic image on ABUS -





- due to the compact tissue within and behind the nipple/areola.



Sebaceous glands

Skin level – ABUS



The sebaceous glands contain sebum





Mammogram of the skin

Perception *and* appreciation of the *four* basic building blocks of the breast on coronal ABUS images *through* comparison with the underlying subgross, thick section (3-D) histology.



A slice 2 mm deep to the skin.



The subcutaneous adipose tissue has minimal structure on the coronal view.

Mammogram of an anatomic specimen



In deeper slices the atrophic glandular tissue starts to emerge, but still, it is the adipose tissue that dominates the picture.

Mammogram of an anatomic specimen



6mm deep to the skin



In this example the atrophic glandular elements (ducts and TDLUs) are hidden within the fibrous tissue.

Mammogram of an anatomic specimen



10 mm deep to the skin





Cooper's ligament-like structures are composed of TDLUs and ducts (glandular tissue) surrounded by ground glass-like homogenous fibrosis with concave contours (fibroglandular tissue).

12 mm deep to the skin



3D histology

ABUS the coronal section

The *four "building blocks"* of normal breast can be well demonstrated, individually, on the reconstructed 2 mm coronal tissue slices:

Terminal ductal lobular units (TDLUs)
Ducts and their branches
Fibrous tissue (collagen)
Adipose tissue

Together, they form a harmonious pattern that will be changed by any kind of pathologic lesion, benign or malignant. The larger the lesion, the easier it is to perceive on the ABUS slices.





 The smaller the lesion, the greater the challenge in detecting a benign or malignant lesion.



The most frequent signs leading to the detection of an abnormality on the 2 mm ABUS slices.



The most frequent signs leading to the detection of an abnormality on the 2 mm ABUS slices.

2) The presence of either fluid *or* solid tissue within the abnormal lesion (cyst, fibroadenoma, cancer, etc.) alters the normal structure. This is visible on ultrasound as a circular/oval defect.



Simple cyst



Breast cancer





The concave contoured ground glass-like fibrosis hides atrophic ducts and TDLUs. Normal.

The neighboring slide shows a disruption of the normal pattern, indicating the presence of an abnormality (continuation on the next slide).
Example 1 continued



ABUS and conventional ultrasound presentation of this 10 mm invasive ductal carcinoma.

Example 2





The coronal view demonstrates a large number of 1mm sized circular-oval densities (TDLUs).

This harmonious image is considerably changed by a cancer.

Example 2 continued



Solitary stellate breast cancer

The most frequent signs leading to the detection of an abnormality on the 2 mm ABUS slices.

3) Combination of architectural distortion and a circular/oval defect ("black hole") centrally.





Normal, mostly adipose tissue.

Demonstration of the architectural distortion caused by cancer as it gradually appears in the 2 mm ABUS slices. (cont. on next slides)

Example 1 continued

Architectural distortion





There is a considerable architectural distortion in the tissue-slice superficial to the cancer, without seeing the tumor mass itself at this level.

Both the tumor mass and the surrounding architectural distortion are obvious on this slice.

Example 1 continued

Architectural distortion and circular/oval defect



Several consecutive slices demonstrate the malignant process and its impact on the surrounding tissue.



Reflections

Description of the problem *and* presenting a potential solution to the difficulty in perception in Pattern I, using 3D automated ultrasound technique (2 mm coronal sections)



61 year old asymptomatic woman, called back from mammography screening for assessment of the asymmetric density in the upper-outer quadrant of her right breast.

> From the Departments of Mammography and Clinical Pathology Falun Central Hospital, Sweden ©









Skin level

2 mm deep to the skin

2mm thick consecutive coronal slices



12 mm deep to the skin

14 mm deep to the skin

2mm thick consecutive coronal slices



12 mm deep to the skin

14 mm deep to the skin

2mm thick consecutive coronal slices



Multislice



AT



Three consecutive 2 mm thick coronal slices





Confirmation of the finding



MRI exam courtesy: Mats Ingvarsson, M.D.













Hand-held ultrasound



Preoperative 14-g core biopsy



Histology exam courtesy: Tibor Tot, M.D.



Histology

10x10 mm solitary invasive ductal carcinoma. Gr 1 & 2 *in situ* carcinoma in the spicules Total extent: 18x15 mm pN 0/2





47 year old woman, called back from mammography screening for assessment of a stellate lesion in the medial portion of the left breast

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Consecutive 2 mm slices of the coronal sections, right breast



Histologic diagnosis (Rt breast): 16x10 mm solitary invasive ductal carcinoma


Consecutive 2 mm slices of the coronal sections, left breast











Histologic diagnosis (Lt breast): Multiple fibroadenomas



Breast MRI





Breast MRI



Slight contrast uptake and a non-specific architectural distortion in the right upper-outer quadrant. Several circular, benign lesions centrally in the left breast

Breast MRI



Slight contrast uptake and a non-specific architectural distortion in the right upper-outer quadrant. Several circular, benign lesions centrally in the left breast





Histology: 16x10 mm solitary invasive ductal carcinoma



3D automated ultrasound





Histology: 16x10 mm solitary invasive ductal carcinoma

Microfocus magnification

Histology

Right breast:16x10 mm solitary invasive ductal carcinoma.pN 0/2



Left breast: Several fibroadenomas



Kirstenbosch botanical Garden, Cape Town, South Africa

42 year old asymptomatic woman, screening examination

From the Departments of Mammography and Clinical Pathology Falun Central Hospital, Sweden ©





3D automated ultrasound, 2 mm consecutive coronal sections











Multislice, left breast



3D automated ultrasound, 2 mm consecutive coronal sections











Multislice cont.





2 mm consecutive coronal sections



D= 11.7mm

Conformation of the finding



Histology of the 14-gauge core biopsy: Invasive ductal carcinoma

Hand-held ultrasound guided 14-g core biopsy



Conformation of the finding





2 mm consecutive coronal sections



12x11 mm solitary, well differentiated, ER/PR receptor positive invasive breast cancer, associated with Grade 2 *in situ* carcinoma. Total disease extent: 14x11 mm.

No LVI, pN 0/2



49 year old woman, called back from mammography screening for assessment of a stellate lesion in the medial portion of the left breast

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3D automated ultrasound, ED 2 mm coronal section





Confirmation of suspected focus

3D automated ultrasound, 2 mm coronal section series



Multislice

Large section histology

Histology: Unifocal carcinoma





Rt breast, lateral view, skin level

2 mm deep to the skin



Detected by 3D automated ultrasound exam, mammographically occult



Detected by 3D automated ultrasound exam, mammographically occult



Multislice 02

3D automated ultrasound,2 mm coronal section





5cm



Right breast, confirmation of the tumor focus



Multislice 02
Hand-held ultrasound



0.747 cm 0.456 cm





Rt

Bilateral unifocal breast cancers

Lt



MRI exam courtesy: Mats Ingvarsson, M.D.



14-gauge core biopsy, right breast



Histology: 7 mm invasive ductal carcinoma









Description of the problem *and* presentation of a potential solution to the difficulty in perception in Pattern IV, using 3D automated ultrasound technique (2 mm coronal sections)



This 46 year old woman, with no family history for breast cancer, felt a thickening in the upper portion of her right breast.



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Example 1





3D automated ultrasound. 2 mm thick coronal slices Falun MAMMO



Falun

3D automated witrasound. 2 mm thick coronalistices



Falun MAMMO Admin Isk 4/25

5 cm

W 230 L: 124 7 / 25 Nipple 58.4 mm



u.sx W 230 L: 124 **8 / 25** Nipple 58.5 mm Skin 14.8 mm











Right breast: 1) OU quadrant breast cysts 2) 80x67x100 mm multiple foci and diffuse enhancement, malignant tumor. No pathologic axillary lymph nodes.







MRI exam courtesy: Nadja Lindhe, M.D.





Hand-held US

Large cancer





Hand-held US

Large cancer



Hand-held US: Tumor diameter 4.81 cm

-- cm Dist 4.81 cm









Diffuse invasive lobular carcinoma















80x40 mm ER/PR positive diffuse and multifocal invasive lobular carcinoma, classic type. The posterior margin of the specimen is involved. pN 0/4





53 year old woman, felt a thickening in the upper-outer quadrant of her left breast

From the Department of Mammography and Clinical Pathology Falun Central Hospital, Sweden

Example 2





No mammographic sign of malignancy is demonstrable



Lt MLO

Lt CC





Spot compression *and* microfocus magnification: vague suspicion for malignancy

3D automated, reconstructed coronal images



Left breast, skin level

Slice 6 (12 mm deep to the skin)

3D automated, reconstructed coronal images



Slice 7

Slice 8

Numerous "black holes" and architectural distortion suggest the presence of multiple cancer foci

3D automated, reconstructed coronal images



Slice 9

Slice 10

The numerous "black holes" and the architectural distortion are persistent in the consecutive 2 mm coronal reconstructed slices

3D automated, reconstructed





Confirmation of the finding: the "black hole" represents one of the malignant foci

3D automated, reconstructed coronal image





Demonstration of an additional malignant focus



Multislice demonstrates the multiple foci




Hand held ultrasound: malignant breast tumor



+ 19.4mm × 16.9mm









14-gauge core biopsy:

Breast MRI diagnosis

- Lt breast with multifocal malignancy. Extent of disease: 90X60X45 mm.
- Pathologic axillary lymph nodes. Findings suspicious for metastases in the skeleton



Mammography - MRI correlation







P-R-A

Left breast sagittal view





P-R

Left breast sagittal view



Large thin section - MRI correlation



Numerous cancer foci, also within the skin

Breast MRI - large thin section histology correlation



Mammography (CC projection) – breast MRI correlation









Numerous invasive lobular carcinoma foci. Histology – breast MRI correlation





Invasive lobular carcinoma, intermediate power image



Slice 10

3D coronal ultrasound /MRI /large section histology correlation



Multiple foci of invasive lobular carcinoma



E-cadherin negative

E-cadherin negative (invasive lobular component)

E-cadherin pos (inv. ductal component)

Metastases in axillary lymph node

High power image of the metastases

Histology

Multifocal invasive lobular carcinoma with ductal components, associated with LCIS and Grade 2 *in situ* carcinoma. Disease extent: 85x55mm. pN 8/8

Outcome Brest cancer death six months after treatment





Sydney Botanical Garden

An approach to solve the perception problem in Pattern V, using 3D automated ultrasound technique (2 mm coronal sections)



37 year old woman, who felt a lump in the upper-outer quadrant of her left breast

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3D automated ultrasound



Cancer focus # 1

Pos axillary node





Cancer focus # 2







Tumor focus # 1 (12x8 mm)

=



Tumor focus # 2



Image courtesy: Nadja Lindhe, M.D.

Left latero-medial horizontal







Preoperative FNAB of the axillary node of the axillary node of the axillary node of the axillary lymph node metastases

Histology

29x13 mm and 12x7 mm poorly differentiated invasive ductal carcinoma foci with LVI. Total extent: 41x20 mm pN 2/4





Evaluation of ABUS as an adjunct to screening with mammography of asymptomatic women with dense breast tissue is a logical next step in developing screening strategies *to reduce the false-negative rate of mammography*



A large-scale clinical trial was needed to study the sensitivity of cancer detection when screening average-risk asymptomatic women with dense breast tissue with digital mammography and ABUS



Design of a trial

This situation is similar to the introduction of low-dose film-screen mammography in the mid 1970's



Design of a trial

It is for this purpose that a multicenter prospective scientific trial was designed by Stephen W. Duffy, Professor of cancer screening in London, UK




Study designer

W. Duffy

Professor of Cancer Screening and Director, Cancer Screening and Aetiology Group, Wolfson Institute of Preventive Medicine, Queen Mary, University of London, Charterhouse Square, London EC1M 6BQ United Kingdom

Hypothesis

Screening asymptomatic women with dense breast tissue using digital mammography (FFDM) and automated ultrasound (AU) will result in significantly higher sensitivity in the detection of breast cancer compared to screening with digital mammography alone with acceptable call-back rates.



Objective

To determine the sensitivity of breast cancer detection *in asymptomatic women with a dense breast pattern* screened with

Mammography and automated ultrasound
Compared to mammography alone





Design of a trial

The study had a matched pair design in which the examination of each woman with dense breast tissue has received a separate interpretation of the digital mammogram only,

as well as a combined interpretation of the digital mammogram and the automated 3-D ultrasound



Design of a trial

This clinical study of asymptomatic women with >50% parenchymal density has assessed the sensitivity and specificity of automated breast ultrasound combined with digital mammography

as a multimodality breast cancer screening method compared to digital mammography alone



Ongoing trial

The evaluation of this study has provided information about the value of digital mammography combined with automated 3D ultrasound as a new, multimodality screening tool in the fight against breast cancer



Playing with water and light