Histological Analysis of Biological Tissues using High- Frequency Ultrasound

K. M. Sorensen

Utah State University, Logan, Utah

T. E. Doyle, B. D. Borget, M. Cervantes, J. A. Chappell, B. J. Curtis,
M. A. Grover, J. E. Roring, J. E. Stiles, and L. A. Thompson

Utah Valley University, Orem, Utah

164th Meeting of the Acoustical Society of America, Kansas City,
MO, 22-26 October 2012

Objective

- Previous findings
 - High-frequency (HF) ultrasound can differentiate between a range of breast pathologies in surgical specimens
 - Two parameters are sensitive to histopathology
- Direction
 - Determine the mechanism linking HF ultrasound to histology
- Approach
 - Review breast specimen results
 - Test range of bovine tissue from heart, kidney, and liver
- Hypothesis
 - Ultrasound sensitivity is a function of the microscopic heterogeneity—and therefore histology—of the tissue

Measurements

Waveform Analysis

Through-Transmission

Pulse Echo

First-Order Spectra

Second-Order Spectra

Surgical Specimens

Benign	Malignant
Lymph nodes	Ductal Carcinomas (DC): <ul style="list-style-type: none"> ● Ductal carcinoma in situ (DCIS) ● DCIS, solid & cribriform ● Invasive ductal carcinoma (IDC) ● DCIS + IDC
Normal breast	
Atypical: <ul style="list-style-type: none"> ● Benign with calcifications ● Atypical ductal hyperplasia ● Fibrocystic change ● Papilloma 	
FN-FA-TA: <ul style="list-style-type: none"> ● Fat necrosis ● Fibroadenoma ● Tubular adenoma 	Lobular Carcinomas (LC): <ul style="list-style-type: none"> ● Lobular carcinoma in situ (LCIS) ● Invasive lobular carcinoma (ILC)
Total measurement positions = 29	Total measurement positions = 26

Breast Histology Correlations

Benign fibroadenoma
(WebPathology.com)

Normal breast tissue
(U. Mich.)

c

- Tissue heterogeneity increases from fibroadenoma (mostly stroma) to LCIS (tumor proliferation in lobules)
- Heterogeneity correlates with peak density, inversely with slope

Surgical Margin Results

- Peak density (number of peaks and valleys) from first-order spectra

- Normalized Slope from second-order spectra

Multivariate Analysis

- Attenuation vs. peak density

- Rotated and translated plot

Statistical Significance

***t*-test results:** Differentiation from normal tissue

Pathology	Peak density	Slope
Lobular carcinomas	$p < 0.02$	$p > 0.20$
Ductal carcinomas	$p < 0.05$	$p < 0.20$
FN-FA-TA	$p < 0.05$	$p < 0.01$
Benign pathologies	$p < 0.10$	$p < 0.01$

One-way ANOVA test: 5% significance level for peak density, close to 1%

Heart Histology Correlations

Cardiac muscle
(Yale Medical Histology)

Muscular artery
(Yale Medical Histology)

- Cardiac tissue displays uniform structure
- Vascular structure is more complex with 3 layers (tunica intima, tunica media, and tunica adventitia), smooth muscle, collagen, etc.

Bovine Heart Results

- Vascular tissue (aorta, vena cava, etc.) shows significantly higher peak densities
- No significant variations observed for normalized slope

Kidney Histology Correlations

Cortex
(Yale Medical Histology)

Medullary collecting ducts
(Yale Medical Histology)

Ureter
(Yale Medical Histology)

- Tissue uniformity decreases from cortex to ureter
- Medulla has uniaxial collecting ducts similar to normal breast glands
- Size of heterogeneities increase from cortex to ureter

Bovine Kidney Results

- Ureter and surrounding fat tissue show significantly higher peak densities
- Renal medulla shows significantly lower normalized slope values

Discussion

- Repeatable correlations shown between tissue heterogeneity and peak density of 1st-order spectra
 - Human breast: Ductal and lobular carcinomas
 - Bovine heart: Vascular tissue
 - Bovine kidney: Ureter and surrounding stroma
- Correlations less repeatable for slope of 2nd-order spectra
 - Slopes are lowest for normal ductal structures
 - Normal breast tissue and medullary collecting ducts
- No correlations seen for liver tissue or between organs
 - Tissue uniformity (liver)
 - Averaging effects (between organs)

Conclusions

- Tissues with greater peak densities in 1st-order spectra exhibit:
 - More complex, less uniform histology
 - Larger or more widespread heterogeneities
- Tissues with lower slopes in 2nd-order spectra exhibit:
 - Normal microscopic ductal structures
 - Examples: Normal breast glands and renal medulla
- Results support hypothesis that HF ultrasound is sensitive to microscopic heterogeneity—and thus histology—in tissues
- Applications
 - Intraoperative evaluation of margins during breast cancer surgery
 - Real-time pathology for other cancers and procedures

Acknowledgments

- Funding support:
 - NIH Grant R21CA131798
 - Utah Valley University Grant for Engaged Learning
- Huntsman Cancer Institute:
 - Leigh Neumayer
 - Rachel Factor
- Utah Valley University:
 - Melissa Monk
 - Ken Slater
- Circle V Meats for donation of bovine organs

Questions?