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QUANTITATIVE ULTRASOUND IMAGING

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OUTLINE

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INTRODUCTION

- **Objective of quantification**
  - **Objective measurement of tissue pathological state by medical imaging plays an increasing role in clinical practice**
- **Quantitative ultrasound imaging**
  - **Ultrasound imaging modality offers dedicated solutions based on signal- or image-derived quantitative measurements for evaluating a variety of diseases in cardiology, radiology and oncology**

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I. WALL MOTION TRACKING

Y. Abe, H. Ohuchi, T. Kawagishi, *Two and three dimensional wall motion analysis*, White Paper Toshiba Medical Review TMR 0805-1.

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I. Wall Motion Tracking

- **Medical context**
  - Echocardiography: cardiac ultrasound imaging
  - Analysis of the cardiac function based on heart motion conceived as an aid to assessment of
    - Ischemia
    - Dyssynchrony
    - Heart failure
    - etc.

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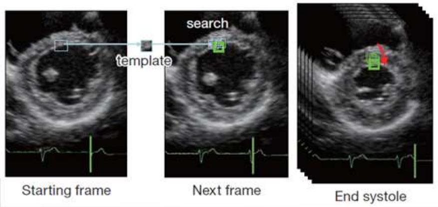
I. Wall Motion Tracking

- **Wall Motion Tracking Technology**
  - Speckle tracking methods based on frame-to-frame correlation
  - Process
    - Create template image in a local region in the starting frame
    - Search for local speckle pattern matching the template in the next frame
    - Derive a movement vector based on the displacement of the region
    - Repeat the process on all frames of one cardiac cycle



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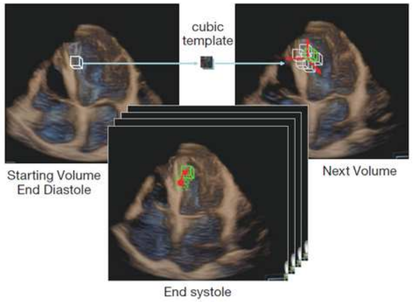
I. Wall Motion Tracking

- **Wall Motion Tracking Technology**
  - Same technique used in 2D applied to 4D data by tracking 3 dimensional cubic templates through the cardiac cycle



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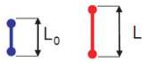
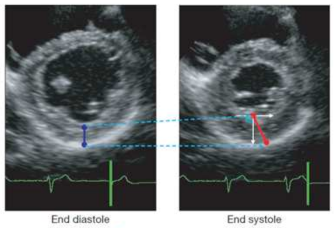
I. Wall Motion Tracking

- **Strain calculation based on tracking results**
  - Strain is the measurement of deformation



$$\text{Strain} = \frac{(L - L_0)}{L_0} \times 100\ [\%]$$

  - Example with radial strain



Relative displacement perpendicular to the endocardium in the short axis view

$$\text{Radial Strain} = \frac{(Lr - L_0)}{L_0} \times 100\ [\%]$$

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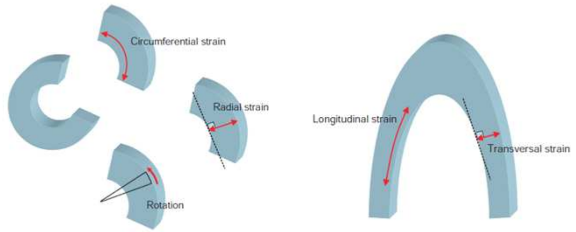
I. Wall Motion Tracking

- **Strain calculation based on tracking results**
  - Strain in different directions for assessment of cardiac motion



Short axis view   Apical view

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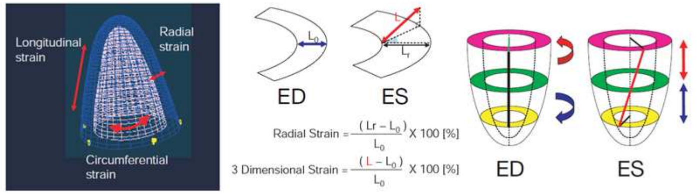
I. Wall Motion Tracking

- **Strain calculation based on tracking results**
  - 3-dimensionnal data offers a comprehensive assessment of the cardiac funtion



a) Conventional Strain   b) Radial 3D strain   c) Torsion

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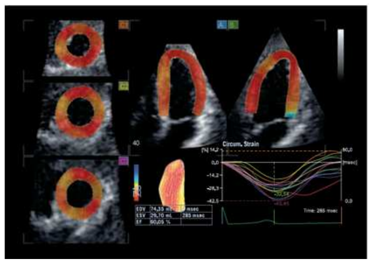
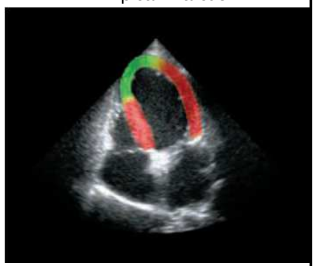
I. Wall Motion Tracking

- **Parametric imaging of strain**
  - Rendering of the spatial distribution of strain using color coding
  - Ultrasound system: Toshiba Artida

Normal case



Apical infarction



Circumferential strain

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II. Tissue Characterization

H. Toyoda, T. Kumada, N. Kamiyama, K. Shiraki, K. Takase, T. Yamaguchi, H. Hachiya, *B-Mode Ultrasound With Algorithm Based on Statistical Analysis of Signals: Evaluation of Liver Fibrosis in Patients With Chronic Hepatitis C*, AJR Am J Roentgenol., 193(4):1037-43, 2009.

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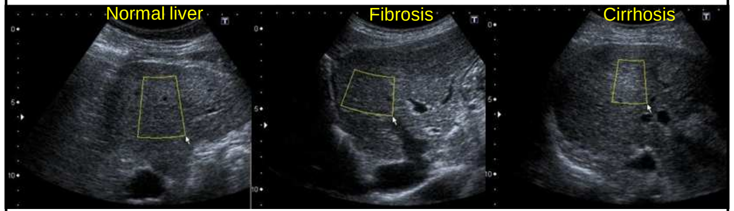
II. Tissue Characterization

- **Principle**
  - Tissue characterization consists in differentiating subtle changes in ultrasound speckle patterns, indicative of the tissue microstructures, which remain non perceptible to human visual inspection
- **Clinical problem**
  - Evaluation of the degree of liver fibrosis in patients



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II. Tissue Characterization

- **Speckle analysis**
  - Definition of ultrasound speckle:
    - Granular pattern in images formed with coherent radiation of scatterers
  - When size of tissue structures < wavelength
    - Probability Density function of echo amplitude = Rayleigh distribution
  - Rayleigh distribution approximation
    - Typical of normal liver tissues (homogenous speckle pattern)
    - No longer valid in fibrotic liver tissues because size of nodules and fibrous structures > wavelength
- **Clinical context**
  - Speckle changes from homogeneous to heterogeneous with progression of liver fibrosis towards cirrhosis
  - Difficult to assess echo amplitude statistics by visual observation
  - Quantitative method of evaluating liver fibrosis would be useful

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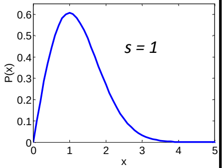
II. Tissue Characterization

- **Rayleigh distribution**

$$\mathrm{P}(x) = \frac{x}{s^2} e^{-x^2/(2s^2)}$$

x : echo amplitude

s : scale parameter



Mean: $\mu = s\sqrt{\frac{\pi}{2}}$ *Variance :* $\sigma_R^2 = \frac{4-\pi}{2} s^2 \Rightarrow \sigma_R^2(\mu) = \left(\frac{4-\pi}{\pi}\right)\mu^2$

- **Chi-square test**
  - Determinate whether a difference exists between the measured variance σ^2 and the ideal variance of Rayleigh distribution

$$C^2 = \frac{\sigma^2}{\sigma_R^2}$$

σ^2 : measured variance

σ_R^2 : ideal variance for homogenous speckle pattern

$C^2 = \mathbf{1}$ means normal liver tissue

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II. Tissue Characterization

- **Modified Chi-square test**
  - Introduction of a threshold α to remove local structures (thin vessels or specular reflectors) from the statistical analysis
  - Only echo-amplitude samples $< \mu + \alpha\sigma$ are selected

Modified variance:

$$\sigma_m^2 = \frac{1}{N_m}\sum_i (x_i - \mu)^2 \Big|_{x_i < \mu + \alpha\sigma}$$

Modified mean:

$$\mu_m = \frac{1}{N_m}\sum_i x_i \Big|_{x_i < \mu + \alpha\sigma}$$

Modified C_m^2

$$C_m^2 = \frac{\sigma_m^2}{\sigma_R^2(\mu_m)} = \left(\frac{\pi}{4-\pi}\right)\frac{\sigma_m^2}{\mu_m^2}$$

x_i : echo amplitude

α : removal threshold

N_m : Number of selected samples

$$\sigma_R^2(\mu_m) = \left(\frac{4-\pi}{\pi}\right)\mu_m^2$$

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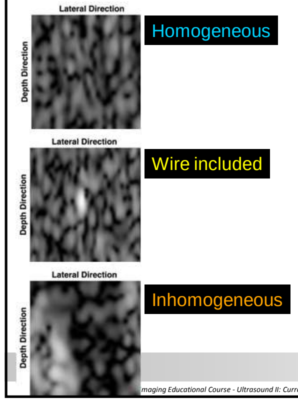
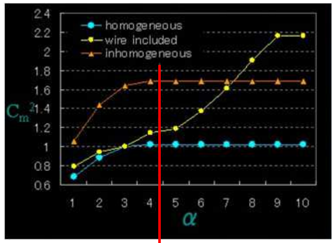
II. Tissue Characterization

- **Determination of the removal threshold α**
  - **Agar phantom mimicking three types of tissue structure**





Optimal: α = 4

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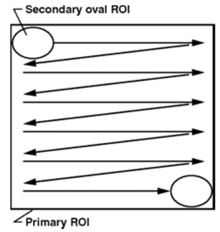
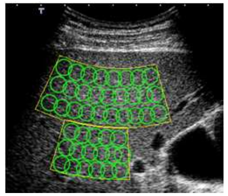
II. Tissue Characterization

- **C_m^2 histogram**
  - **Two level of regions of interest (ROIs)**
    - Primary ROI manually defined to avoid large vessels
    - Secondary ROI automatically sweeping within the primary ROI
  - **Histogram based on multiple values of C_m^2 in secondary ROI**





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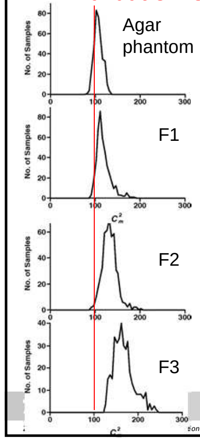
II. Tissue Characterization

- **Validation for Patients with Chronic Hepatitis C**



Fibrosis grades:

F0 = no, F1 = mild, F2: moderate, F3: severe

Patient database:

148 patients with histologically proven chronic hepatitis C

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II. Tissue Characterization

- **Summary**
  - **In B-mode images, speckle pattern changes from homogeneous to heterogeneous with progression of liver fibrosis**
  - **Quantification of homogeneity based on statistical chi-square test of the echo amplitude**
    - Ratio between the measured variance and the ideal variance (Rayleigh distribution)

$$C_m^2 = \frac{\sigma_m^2}{\sigma_R^2(\mu_m)}$$

  - **C_m^2 histogram obtained from multiple secondary ROIs (automatic) within a primary ROI (manual)**
  - **Base on the analyses on 148 patients, mode of C_m^2 histogram may reflect the progression of liver fibrosis**

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III. Contrast Enhanced Ultrasound

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III. Contrast Enhanced Ultrasound

- **Clinical context**
  - Dynamic Contrast Enhanced Ultrasound (DCE-US) utilizes an intravenous injection of microbubble contrast agent, which supports ultrasound imaging of macro-vascularization
  - DCE-US has become an established technique for characterizing focal lesion in liver (Europe)
  - D-CEUS technique is a promising application for monitoring tumor response to cancer therapies
- **Perfusion quantification**
  - Approach uses a mathematical function to model the contrast uptake (or time-intensity-curve) in a region of interest outlining a tumor
  - Derived quantitative parameters are indicative of blood flow dynamics, which are expected to vary during the course of the therapy

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III. Contrast Enhanced Ultrasound

- **Example in small animals**
  - Radiofrequency ablation in rat subcutaneous model tumor model
  - Ultrasound system: Toshiba Aplio

Clip courtesy of Dr. Exner, Case Western Reserve University

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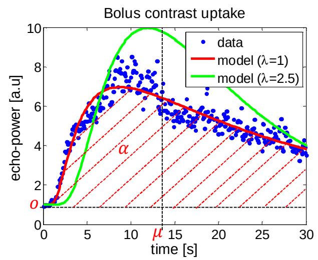
III. Contrast Enhanced Ultrasound

- **Bolus contrast uptake (modeling)**
  - <u>Perfusion model</u>: Local Density Random Walk function[1,2]

$$f(t) = o + \alpha\left(\frac{e^{\lambda}}{\mu}\right)\left(\frac{\lambda}{2\pi}\right)^{1/2}\left(\frac{\mu}{t}\right)^{1/2} e^{-\frac{1}{2}\lambda\left(\frac{\mu}{t}+\frac{t}{\mu}\right)}$$

with

f : perfusion model
t : time variable
o : baseline
α : area under the curve
λ : skewness
μ : transit time



1. Bogaard JM, Jansen JR, von Reth EA, Versprille A, Wise ME., *Random walk type models for indicator-dilution studies: comparison of a local density random walk and a first passage times distribution*, Cardiovasc Res., 20(11):789-96, 1986.
2. Wise ME, *Tracer dilution curves in cardiology and random walk and lognormal distributions,* Acta Physiol. Pharmacol. Neerl., 14:175–204, 1966

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III. Contrast Enhanced Ultrasound

- **ImageLab (research software program)[1]**
  - **Derive Time Intensity Curves (TICs) within Regions of Interest (ROIs) from a sequence of ultrasound contrast images, acquired on TOSHIBA Aplio/Xario ultrasound systems**

1. Developed by Naohisa Kamiyama, PhD - TOSHIBA Medical Systems Corporation Corp.

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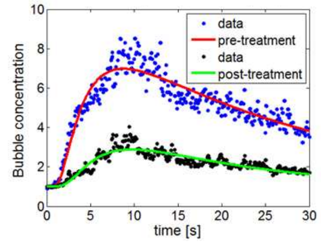
III. Contrast Enhanced Ultrasound

- **Example of perfusion quantification**



Blood volume reduction

in tumor (post treatment) = 47%

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III. Contrast Enhanced Ultrasound

- **Example of current clinical research in oncology**
  - **Evaluation of tumor response to drug therapies by the Institut Gustave-Roussy (Paris, France)**
    - N. Lasseau *et al.*, *Advanced Hepatocellular Carcinoma: Early Evaluation of Response to Bevacizumab Therapy at Dynamic Contrast-enhanced US with Quantification —Preliminary Results*, Radiology, 258(1):291:300, 2011
  - **Protocol (42 patients)**
    - DCE-US performed before and after treatment (3, 7, 14 and 60 days)
    - Measurement of TIC in the rumor using CHI-Q quantification software (Toshiba)
    - Estimate of parameters from TIC by fitting a dedicated perfusion model
  - **Findings**
    - Changes in tumor vascularity can be detected after treatment
    - DCE-US may be useful for quantifying tumor response to therapy
    - Perfusion quantification is a promising tool for predicting tumor response and measure the effectiveness of therapy

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Conclusion

- **Summary**
  - **Quantification in ultrasound imaging offers objective measurements of variety of diseases**
    - Wall Motion Tracking for the analysis of the cardiac function
    - Tissue Characterization for assessing degree of liver fibrosis
    - Contrast Enhanced Ultrasound for evaluating tumor response to therapy
- **Future trends**
  - **Ultrasound molecular imaging**
    - Detect molecular markers that are hallmarks of disease on the intravascular endothelium (eg. vascular endothelial growth factor: VEGF)
    - Targeted microbubbles: ligand attached to the surface of the shell
    - Imaging of tumoral angiogenesis by active targeting
  - **Drug delivery**
    - Incorporation of a drug in microbubbles for local delivery to a target site
    - Microbubbles can induce permeability of the endothelial layer, allowing to increase efficiency of drug delivery at the location of the US beam

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THANKS FOR YOUR ATTENTION!

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