MR-Elastography
Viscoelastic properties of tissue
Clinical application to liver

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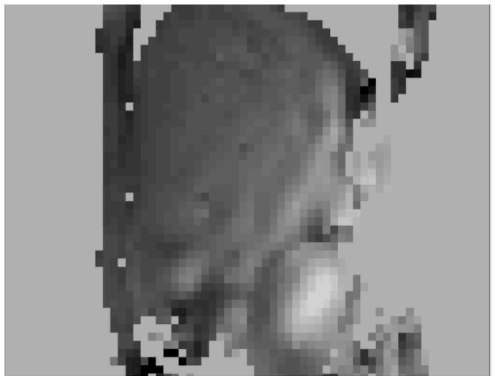


- Hôpital Beaujon, Paris, France
- NIH Bethesda, Washington DC, USA
- Hôpital St. Luc, Brussels, Belgium
- Hôpital Erasme, Brussels, Belgium
- University of Minnesota, Minneapolis, USA
- Institut for Informatics, Oslo, Norway

Starting Point

Q: Does Elastography allow to measure only elasticity and viscosity ?

A: yes and no

Real tissue with
• hierarchical architecture
• presence of vascular system

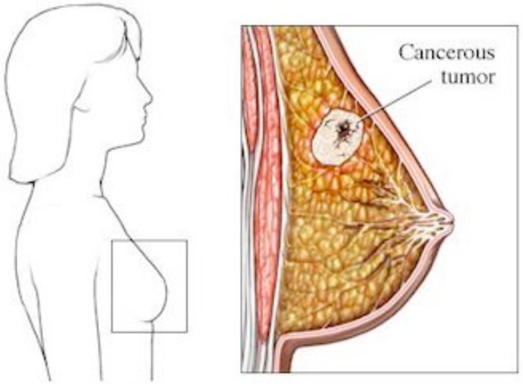
Simple, ideal materials

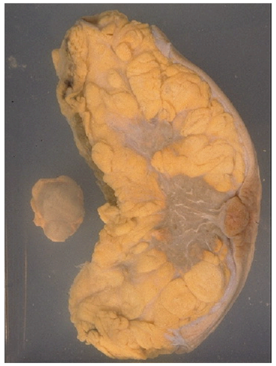
Provides an enormous potential for further research

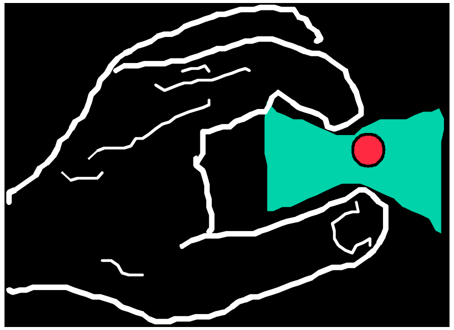
Why ? Motivation for Elastography

Pathological changes are typically accompanied by changes in tissues elasticity

- Breast cancer
- Prostate cancer
- Liver fibrosis



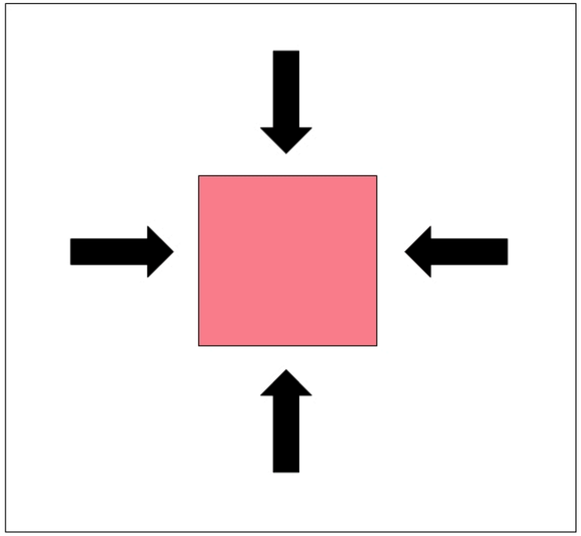




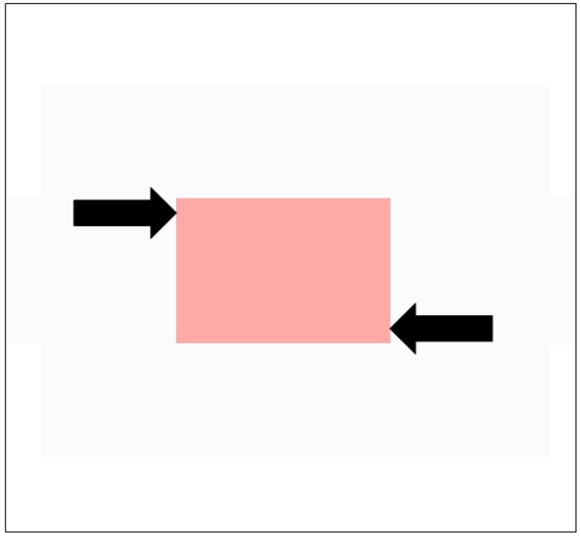
Thus, palpation is rather important for diagnosis,
BUT
sensitivity/specificity is limited due to subjectivity and location/size of lesion

But how to measure elasticity ?

probing elasticity ←→ deforming the object



compression

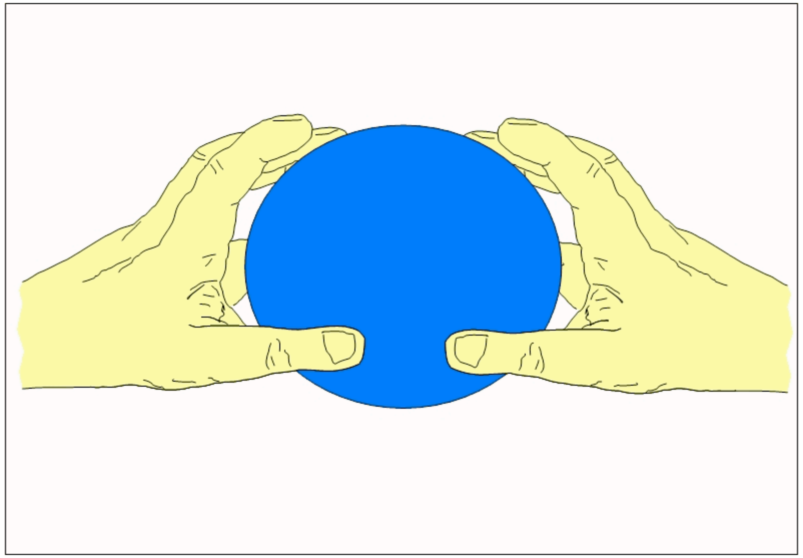


shear

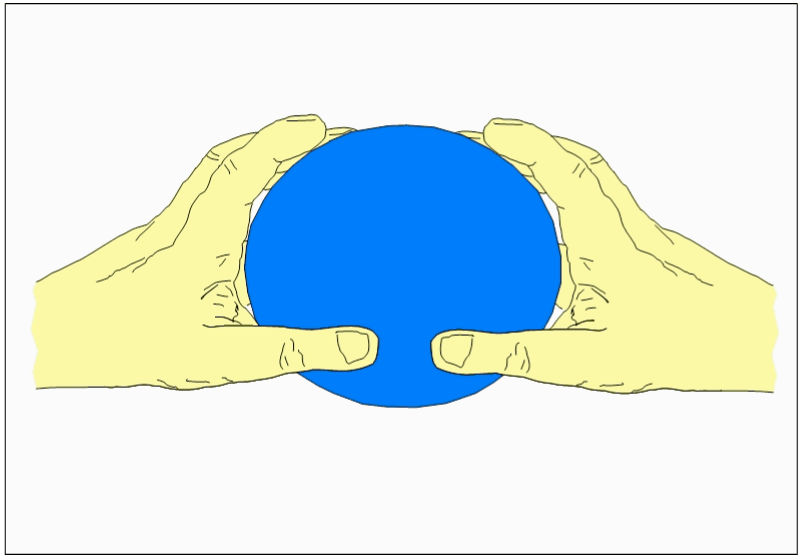
- same force applied from all sides
- volume is changed
- shape is NOT changed

- unbalanced forces
- shape is changed
- volume is NOT changed

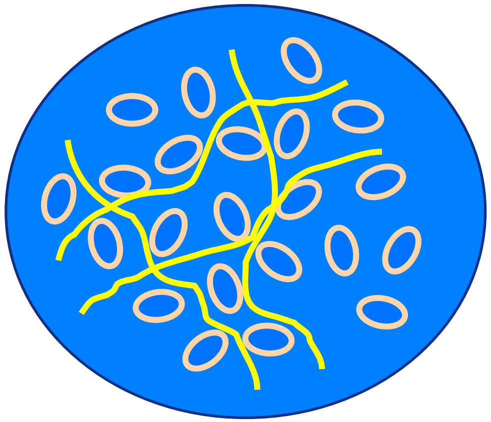
Tissue: about 70% water



compression



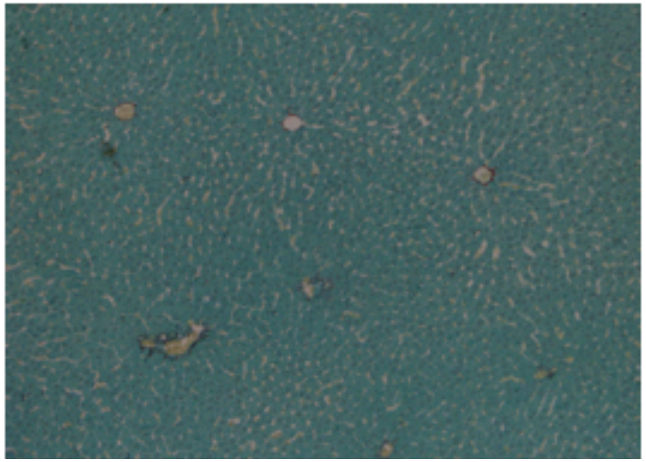
shear



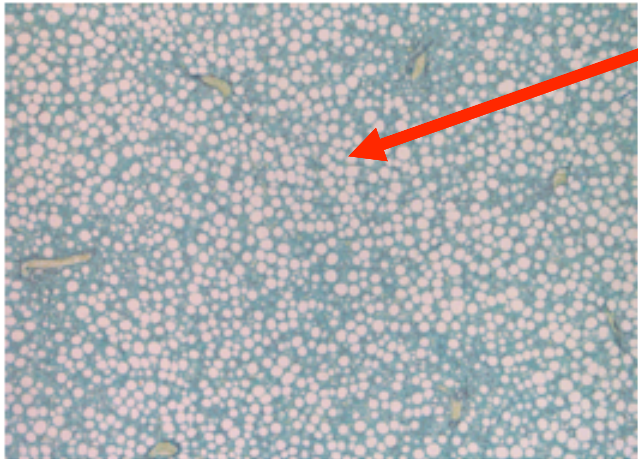
probing the mechanical
structural properties
of the SOLID components
requires to apply SHEAR
deformation

rat

FIBROSIS - NASH: Sirius red staining

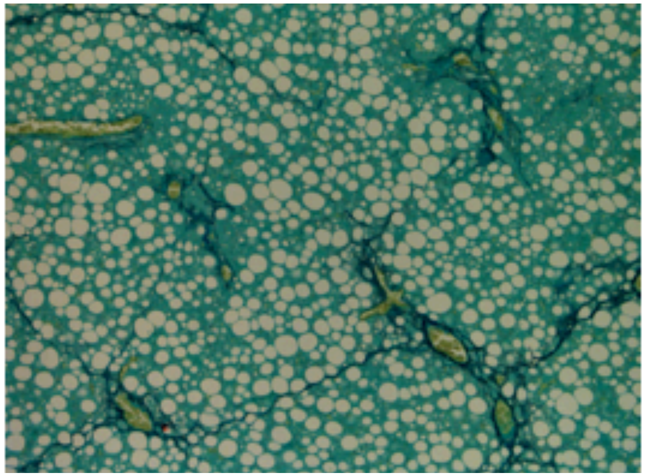


normal

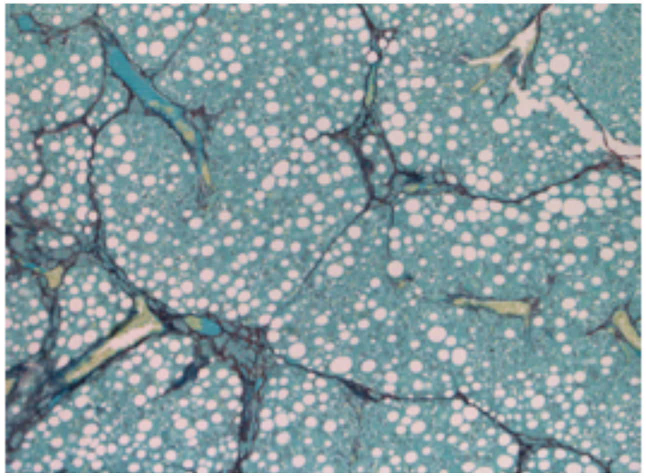


2 weeks after diet

Steatosis
homog.
distributed



5 weeks



8 weeks

Fibrosis $\Uparrow$

Homog. of
steatosis $\Downarrow$

FIBROSIS - Motivation

- Liver fibrosis and cirrhosis is an increasing health problem, because of the increasing frequency of hepatitis C infection in the whole world

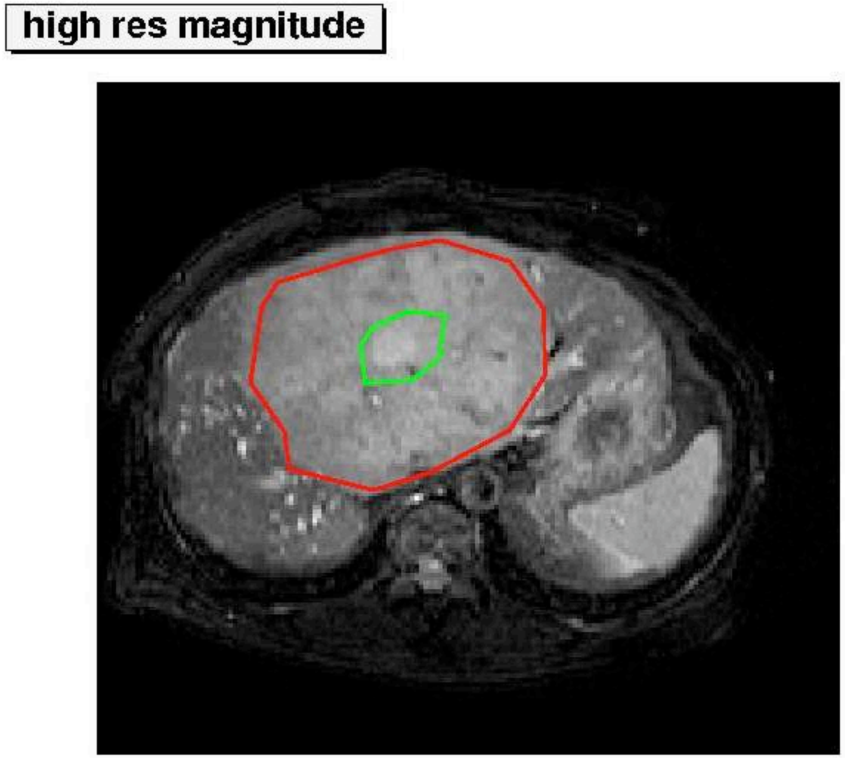
- Currently, the diagnosis and grading of liver fibrosis and cirrhosis can only be made with histopathological analysis of biopsy samples

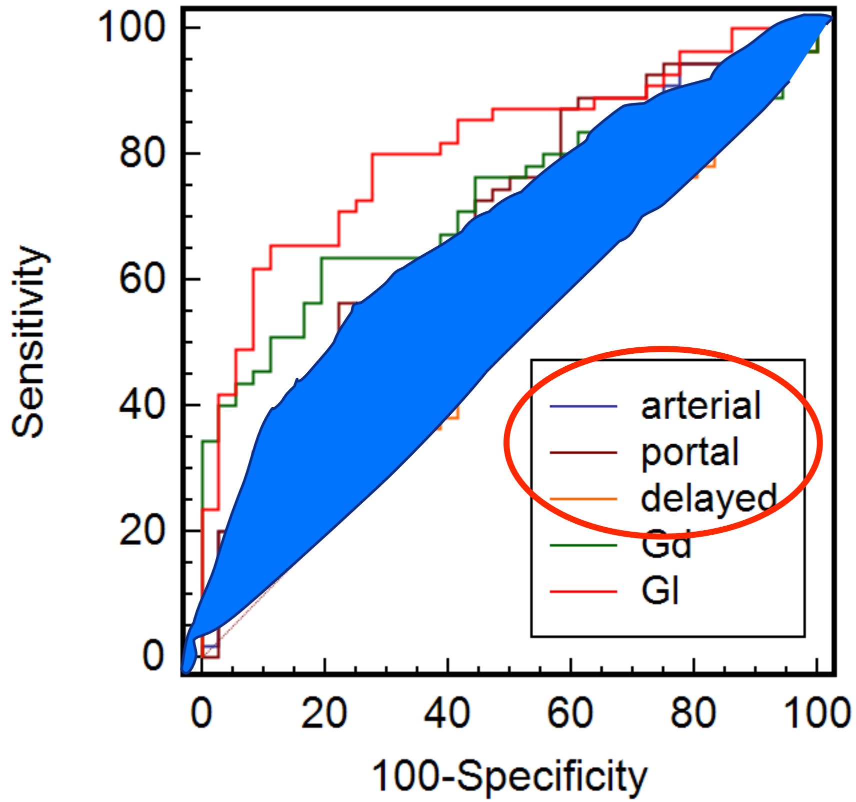
- New treatments to prevent (antiviral therapy) or treat (antifibrotic therapy) fibrosis and cirrhosis are developed

- To assess the efficacy of these treatments without repeating invasive liver biopsies, new, non-invasive diagnostic methods should be developed

Tumor - Motivation

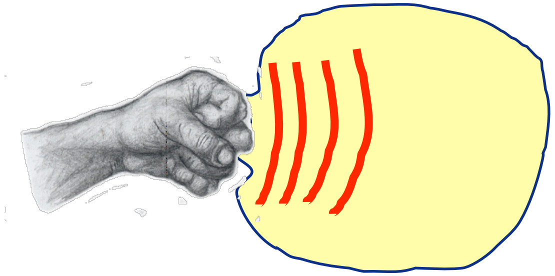
Hepatocellular carcinoma is the 3rd leading cause of cancer mortality worldwide.



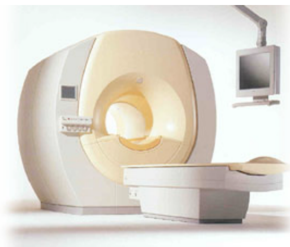


General Concept of Elastography

1. Deform somehow your object



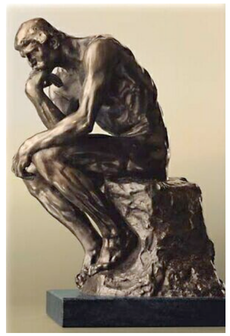
2. Measure the deformation and/or the waves by an imaging technique which is sensitive to motion (MRI, Ultrasound)



=

3. Reconstruct from the displacement field viscoelastic properties

$$\begin{pmatrix} \sigma_{xx} \\ \sigma_{yy} \\ \sigma_{zz} \\ \sigma_{xy} \\ \sigma_{xz} \\ \sigma_{yz} \end{pmatrix} = \begin{pmatrix} \lambda+2\mu & \lambda+\frac{\sigma\Delta}{(1+\sigma)(1-2\sigma)} & \lambda+\frac{\sigma\Delta}{(1+\sigma)(1-2\sigma)} & & & \\ \lambda+\frac{\sigma\Delta}{(1+\sigma)(1-2\sigma)} & \lambda+2\mu & \lambda+\frac{\sigma\Delta}{(1+\sigma)(1-2\sigma)} & & & \\ \lambda+\frac{\sigma\Delta}{(1+\sigma)(1-2\sigma)} & \lambda+\frac{\sigma\Delta}{(1+\sigma)(1-2\sigma)} & \lambda+2\mu & & & \\ & & & \mu & & \\ & & & & \mu & \\ & & & & & \mu \end{pmatrix} \begin{pmatrix} u_{xx} \\ u_{yy} \\ u_{zz} \\ 2u_{xy} \\ 2u_{xz} \\ 2u_{yz} \end{pmatrix}$$



3D Wave equation @ micro-scale

$$2 = \Xi F \partial^2 I + \vec{u}\,\Phi\,\vec{u}\,\vec{u}\,T\,F\,\infty \qquad ()()$$

force
term

source of
contrast in
waves and
what we seek
to reconstruct

about 6 orders
of magnitude
bigger than μ

goes with
(1-2σ) <<< 1

only shear
wave is
attenuated

Hugeness of λ is
balanced by smallness
of $\nabla(\nabla\vec{u})$ due to σ

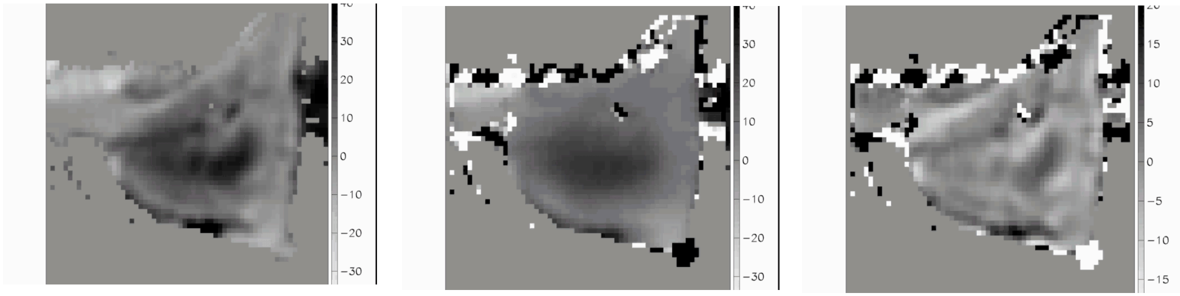
important !!!

Reconstruction: Solution → curl

Apply curl to Eq., because:

$$\vec{u}_{tot} = \vec{u}_L + \vec{u}_T$$

$$\vec{u}_L = \nabla \phi \qquad \vec{u}_T = \nabla \times \vec{v}$$



$$\vec{q} = \nabla \times \vec{u}$$

remember:

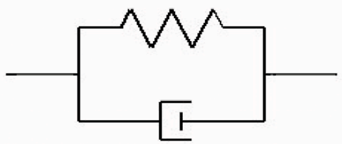
$$\nabla \times (\nabla \phi) \equiv 0$$

$$2 \equiv F \vec{T}^{*} \vec{q} G q \quad ()$$

$$= + G i_{al} G \vec{q}$$

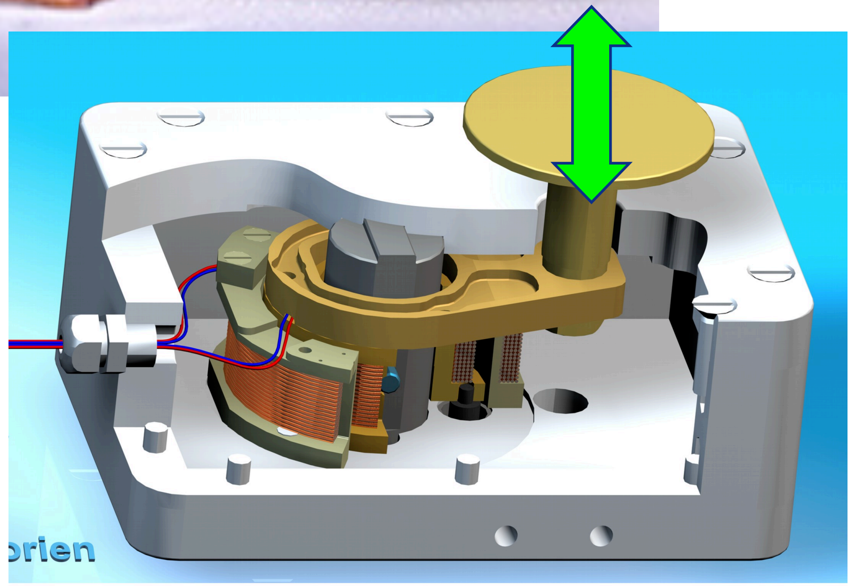
$$= \phi I + T q l i q$$

this interprets the data in terms of the Voigt model, i.e.



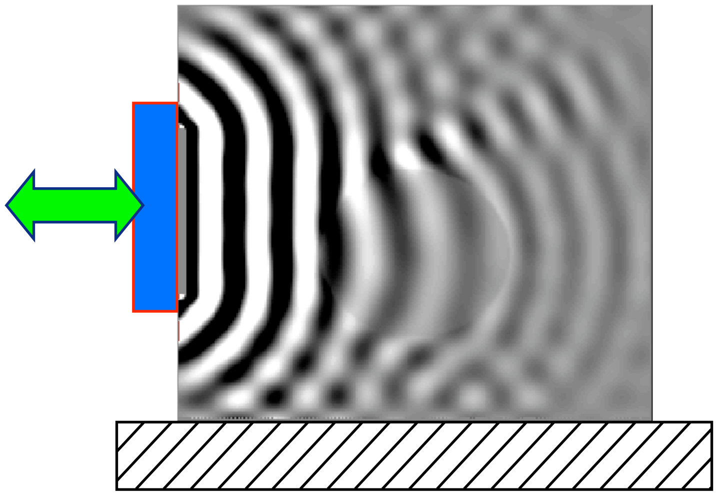
1 st step

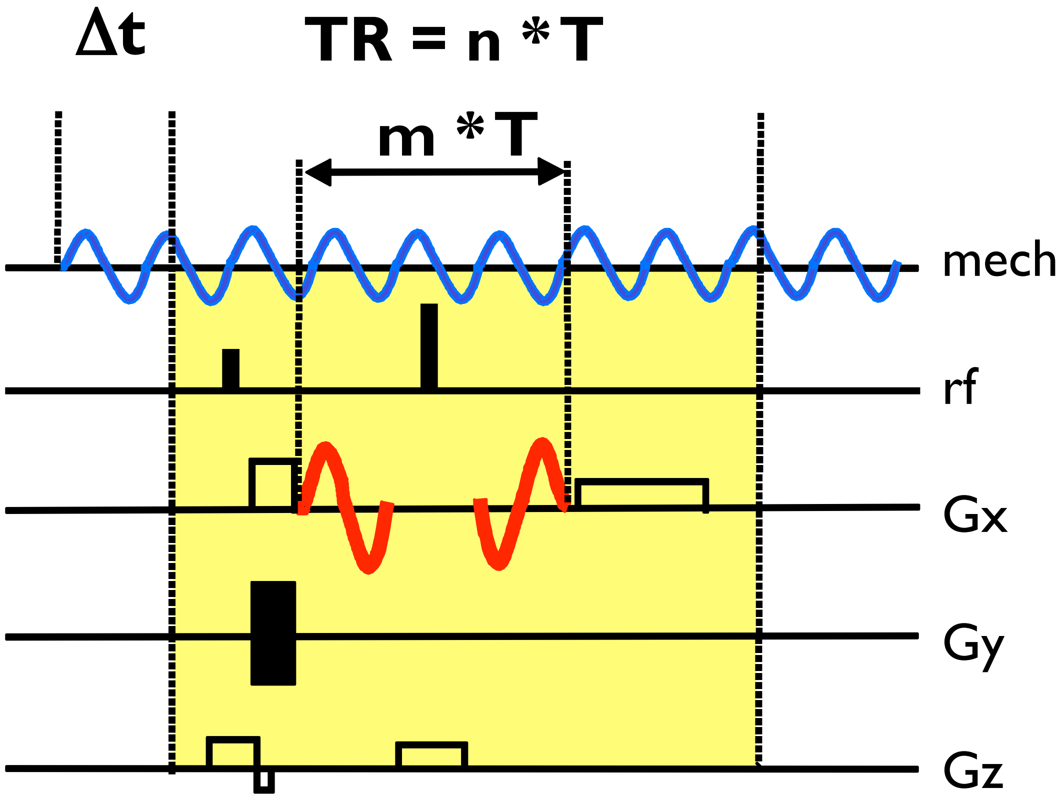
Patient Positioning and Transducer



MR-Sequence: Steady State Excitation

apply mechanical oscillation of ν = 50-100 Hz

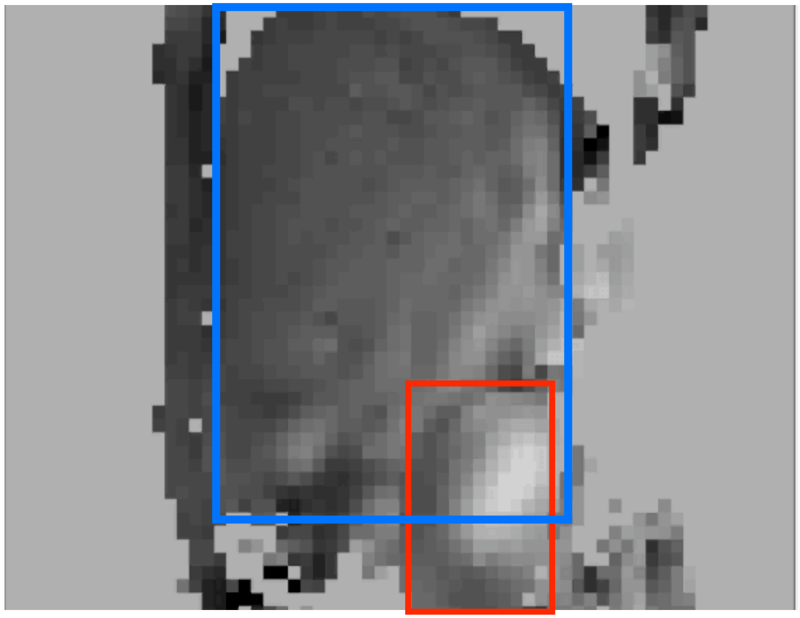




Capture mechanical wave via motion sensitive sequence

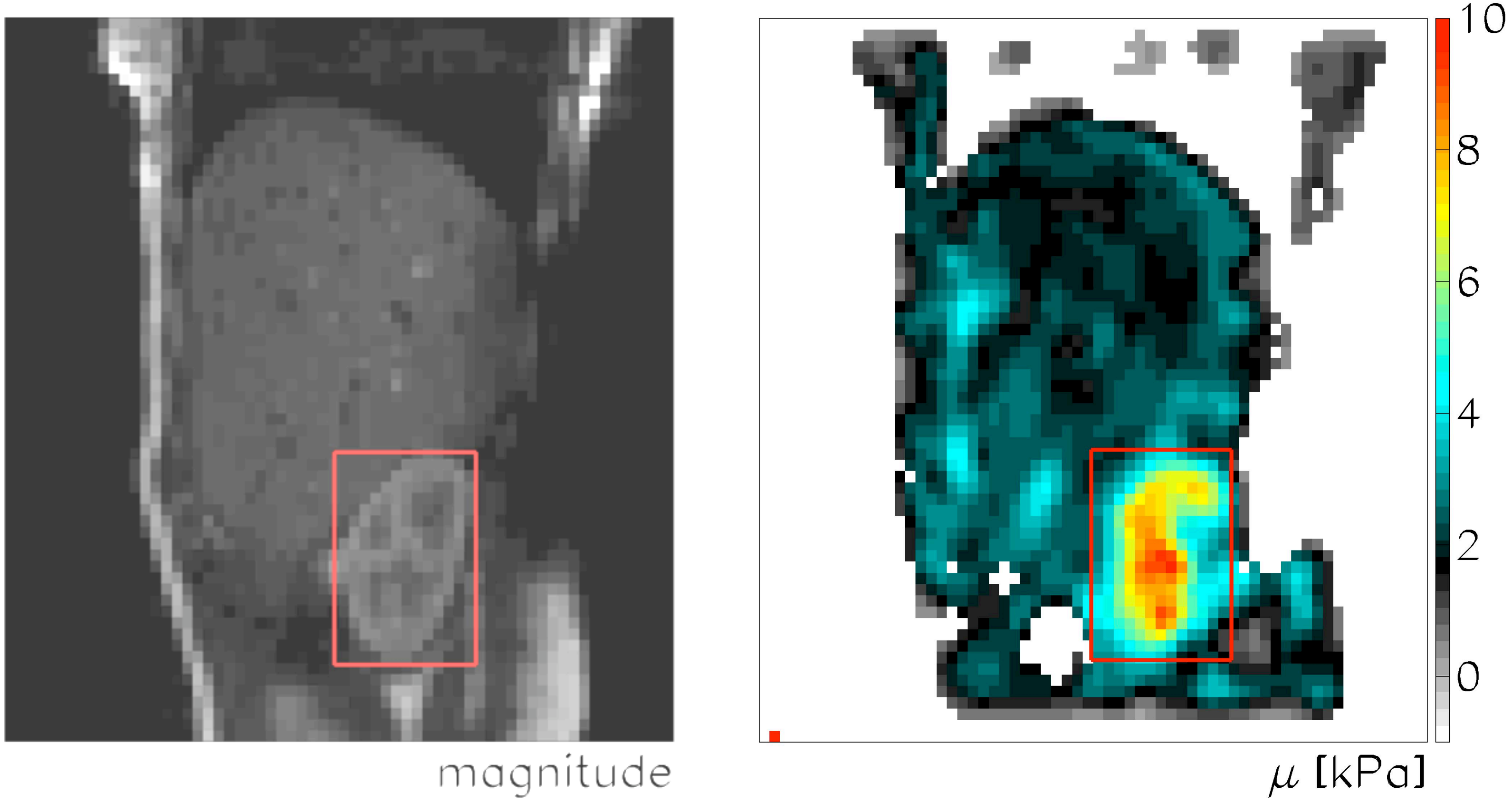
Volunteer: 1min DAQ-time, 3BH

magnitude

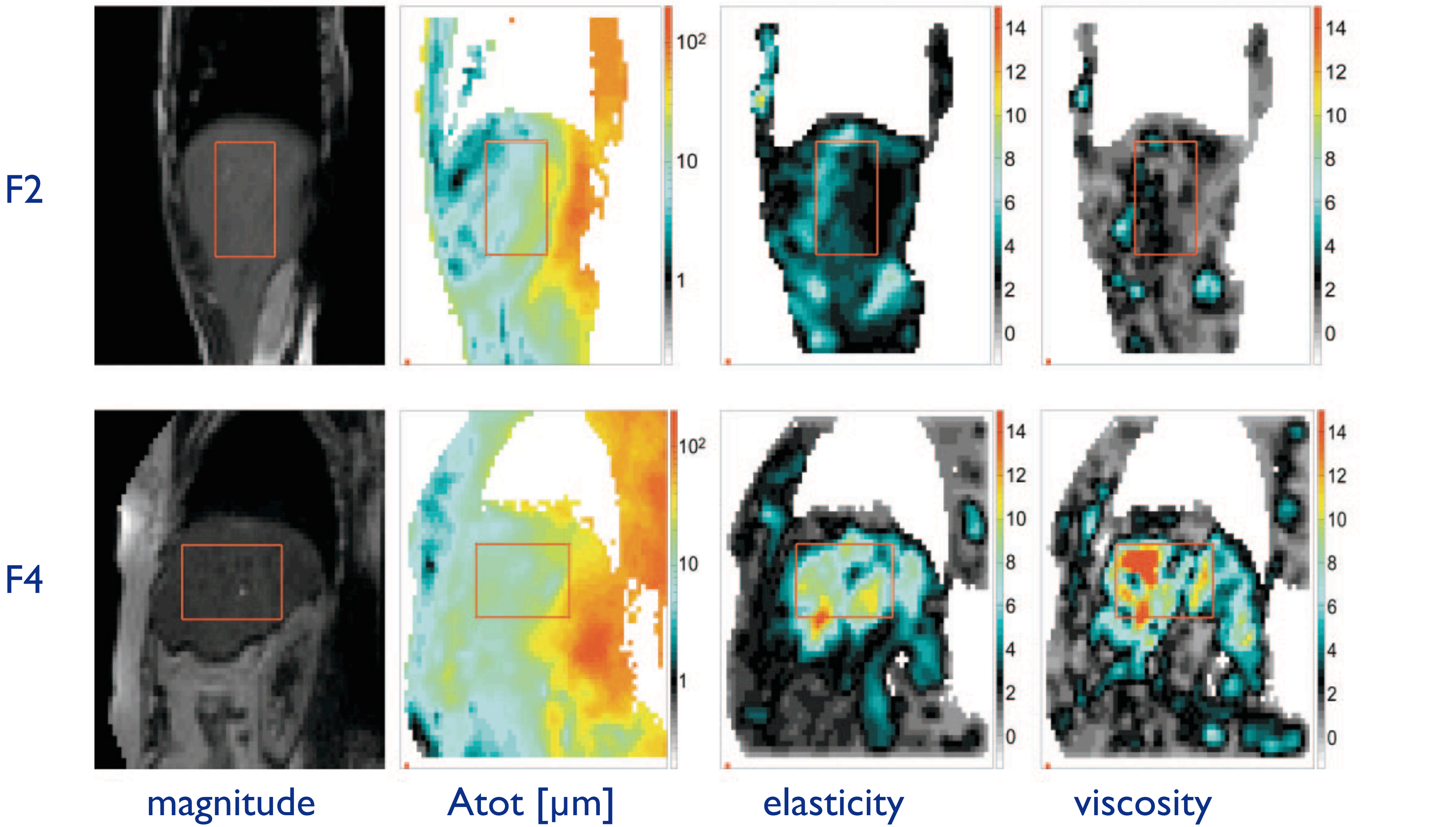


Uz

Volunteer

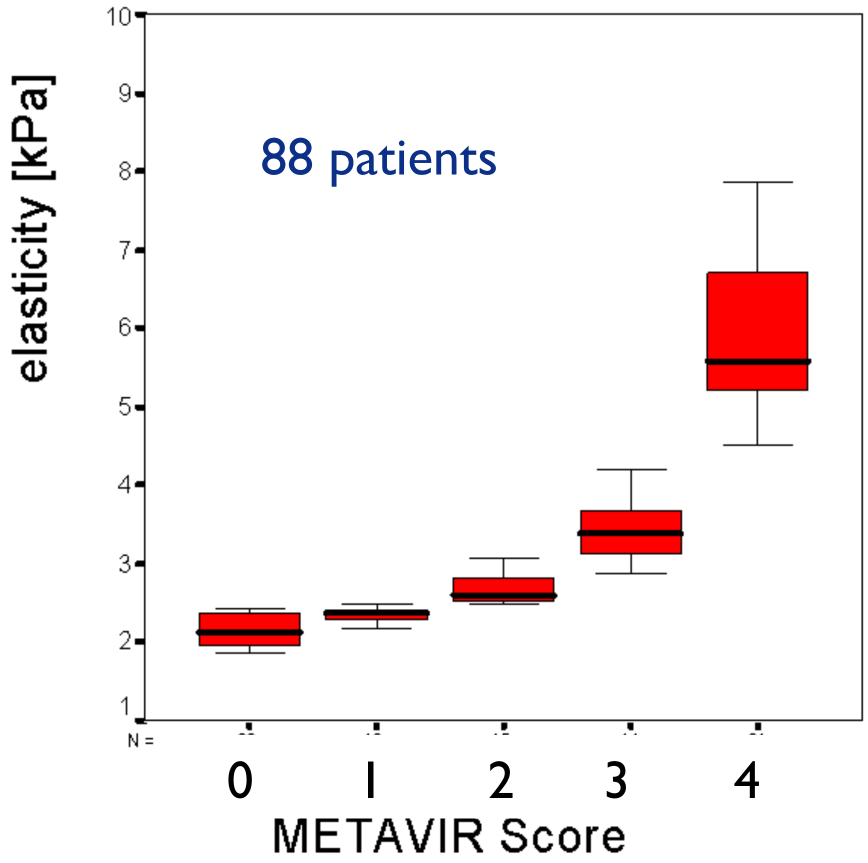


Liver Fibrosis Patients

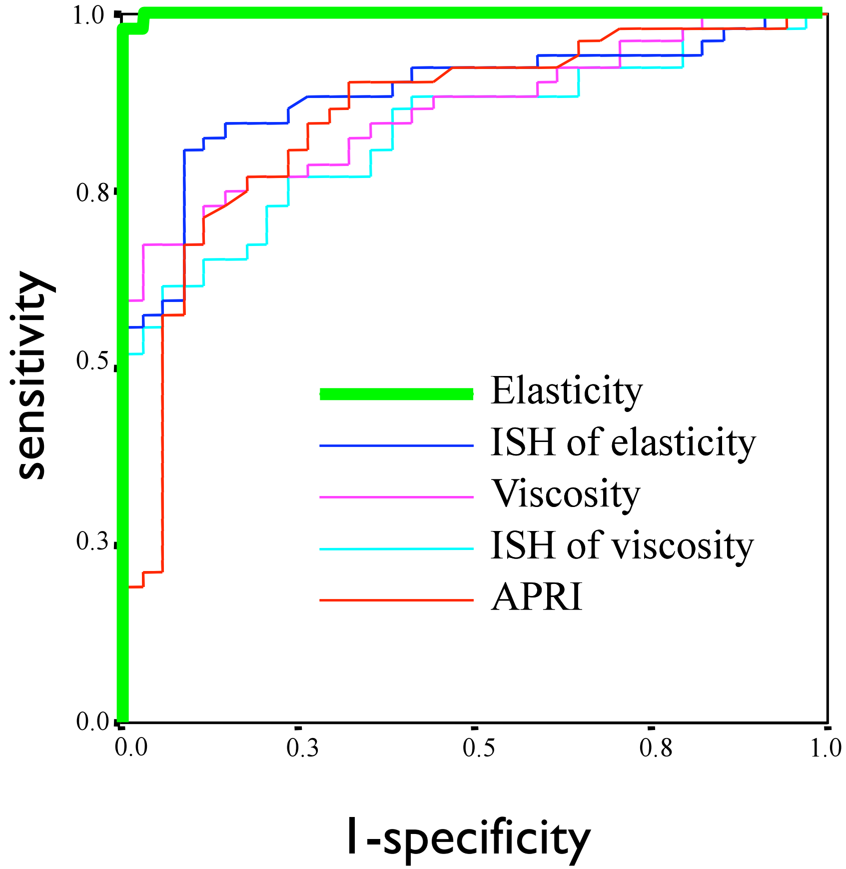


human

Status Clinical Validation

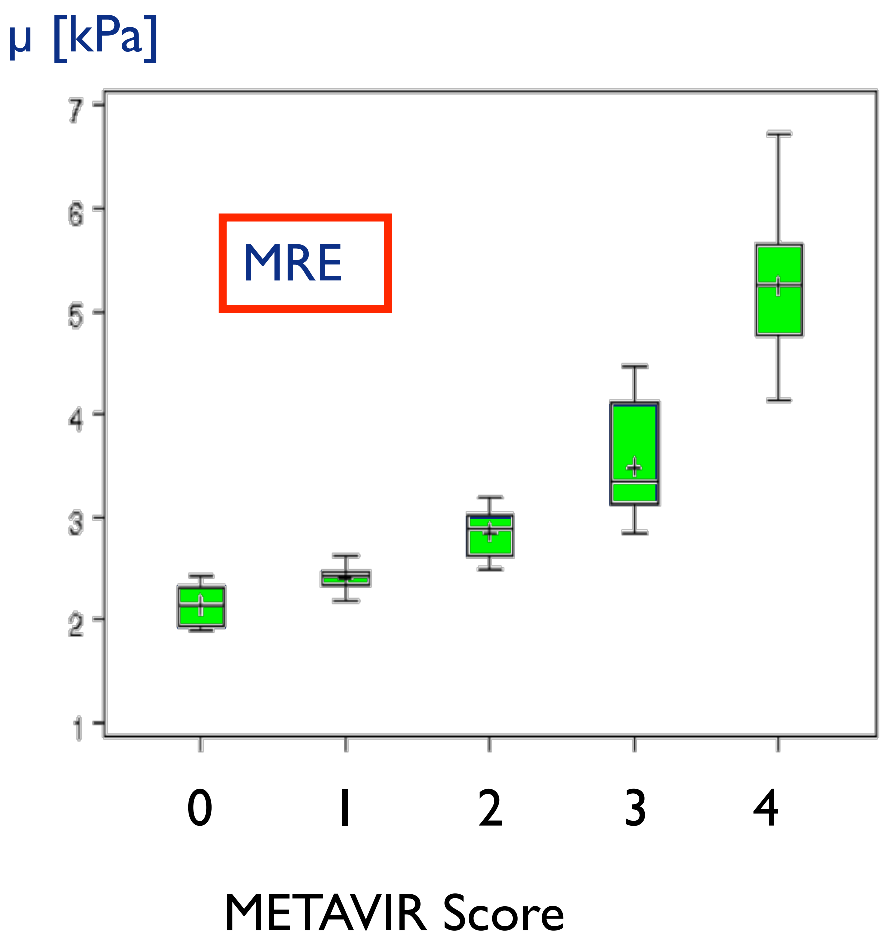


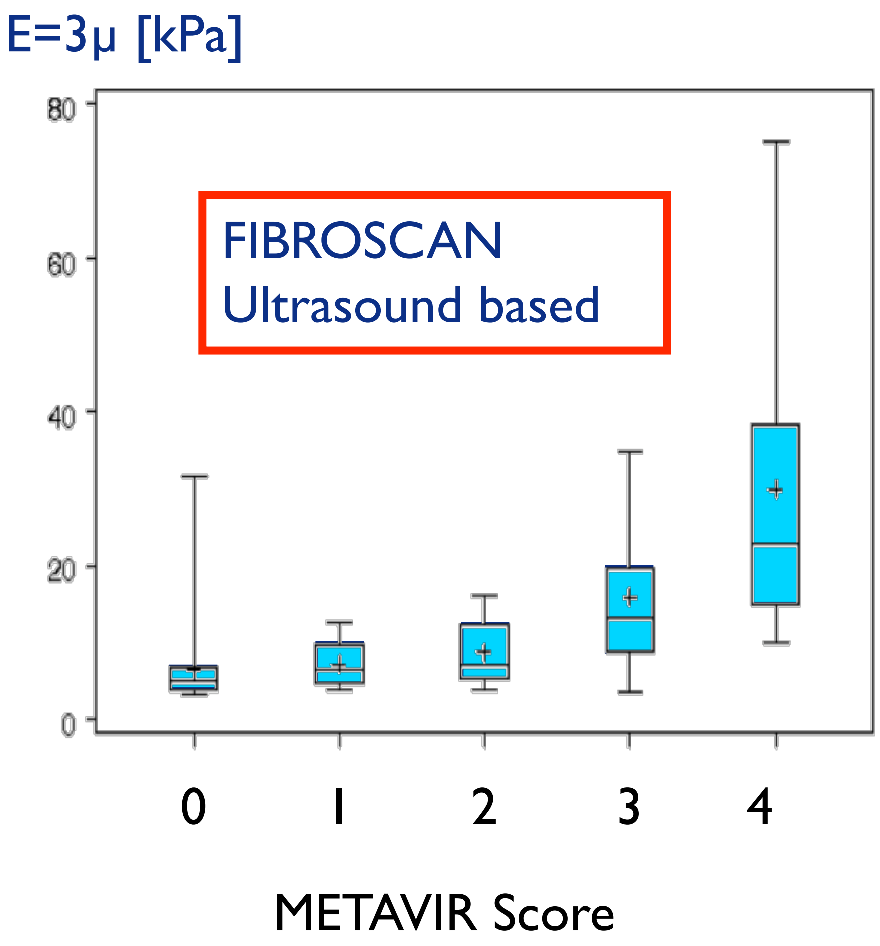
F0-F1 versus F2-F4



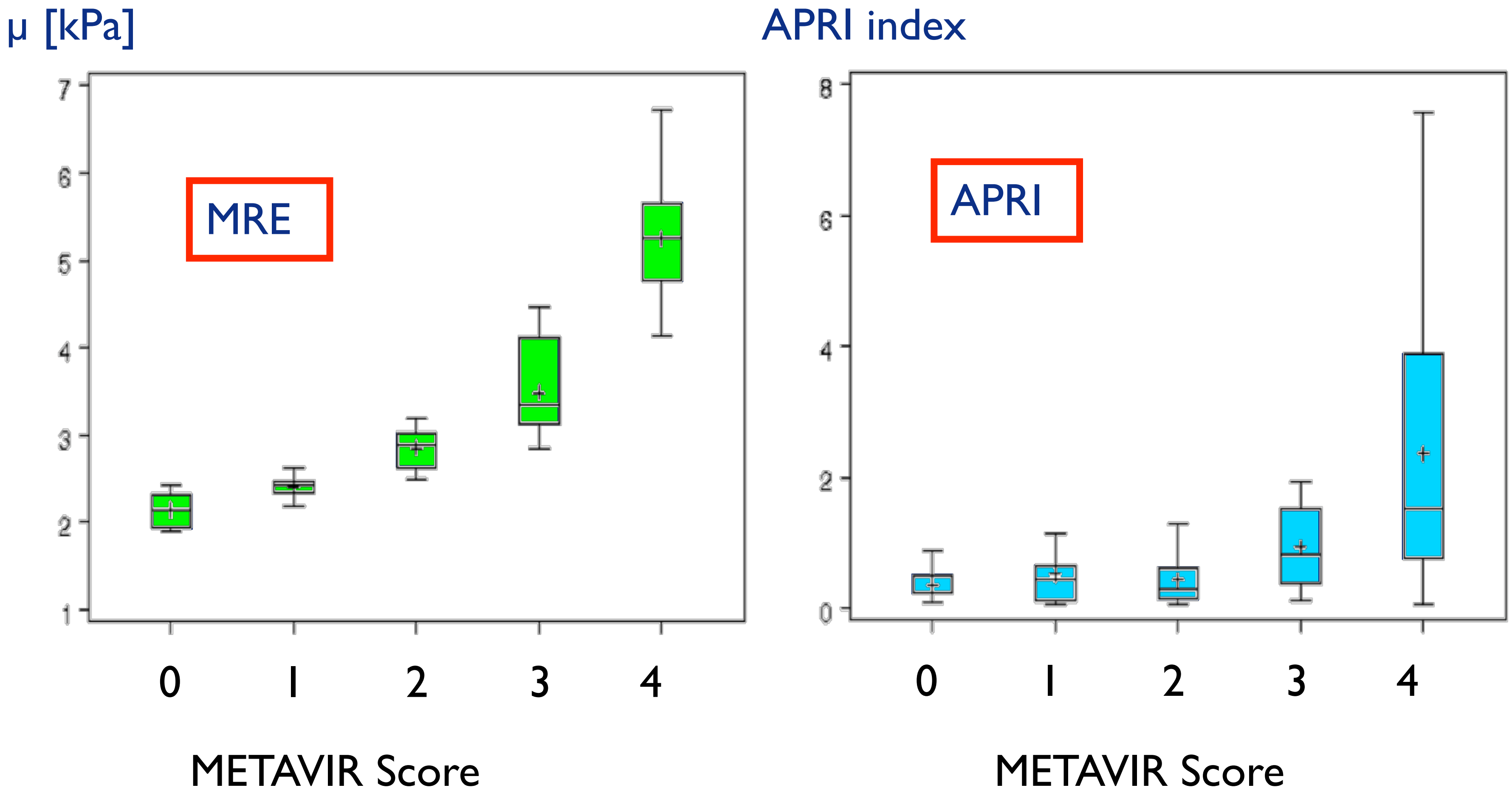
human

Comparison with FIBROSCAN®

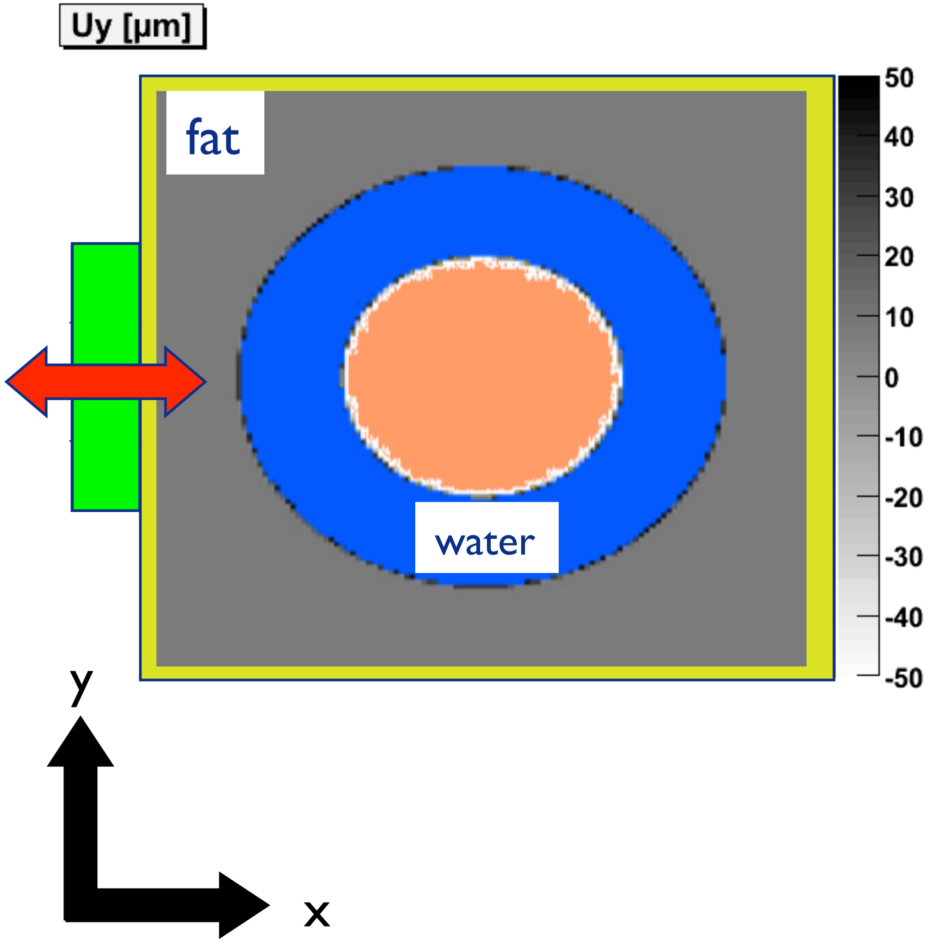


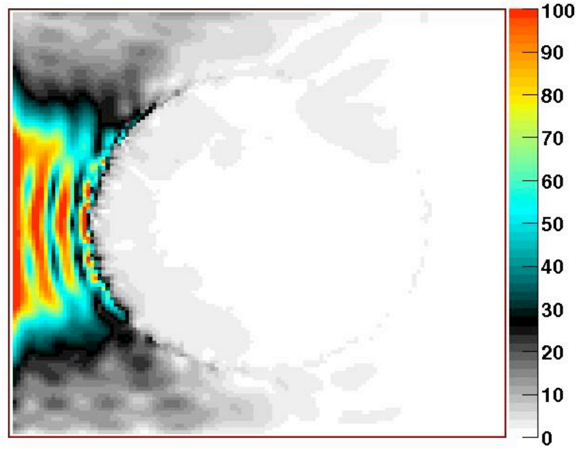


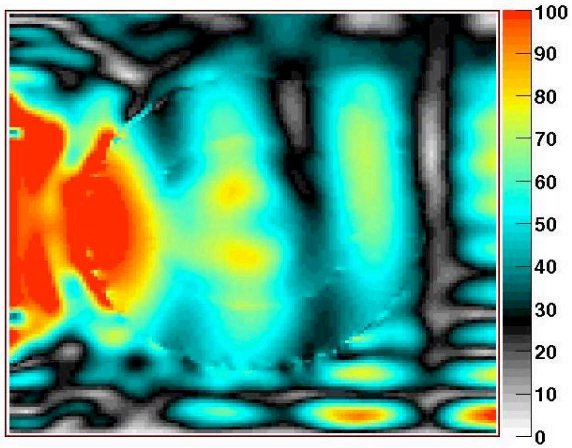
Comparison with APRI



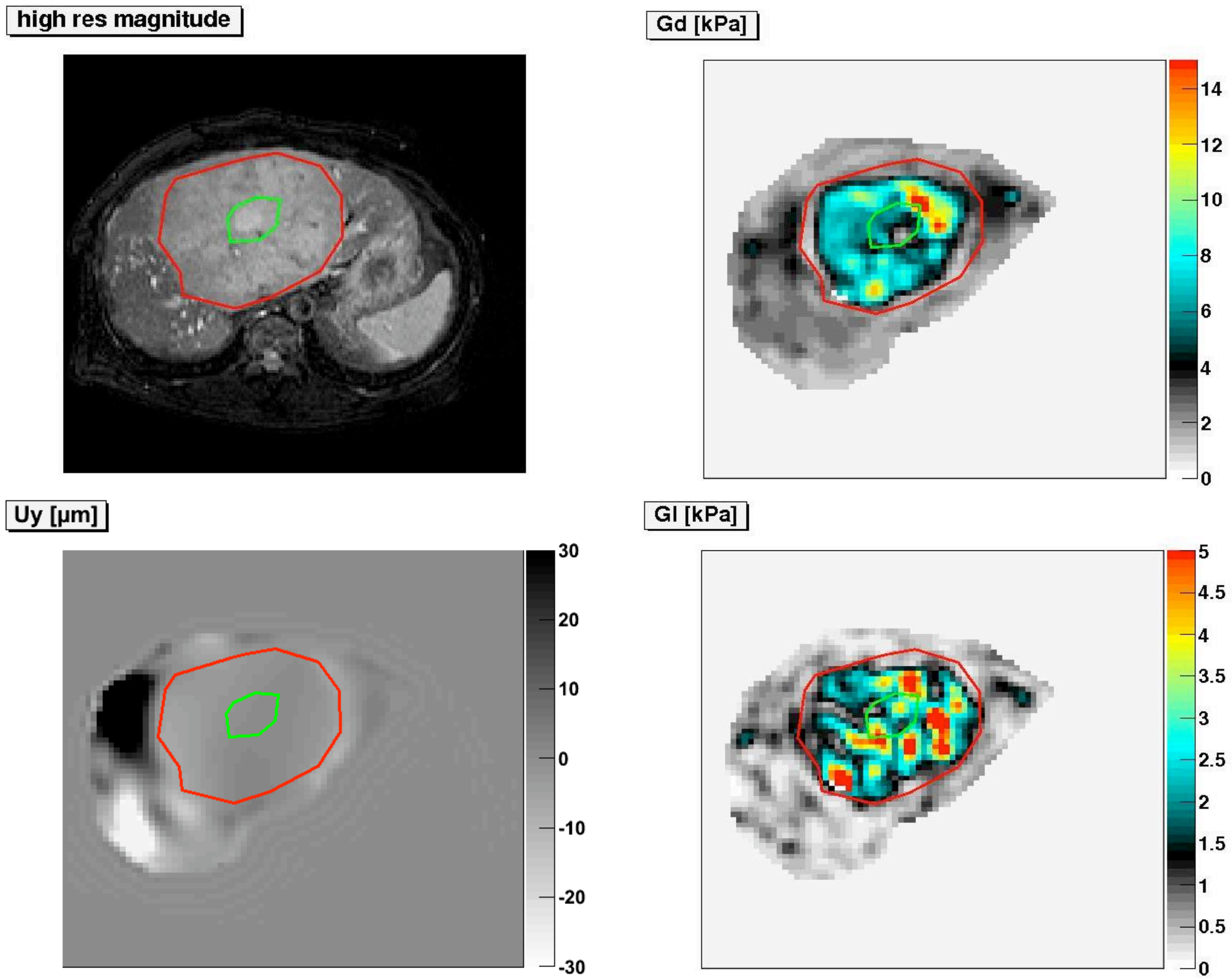
Challenge regarding acitis



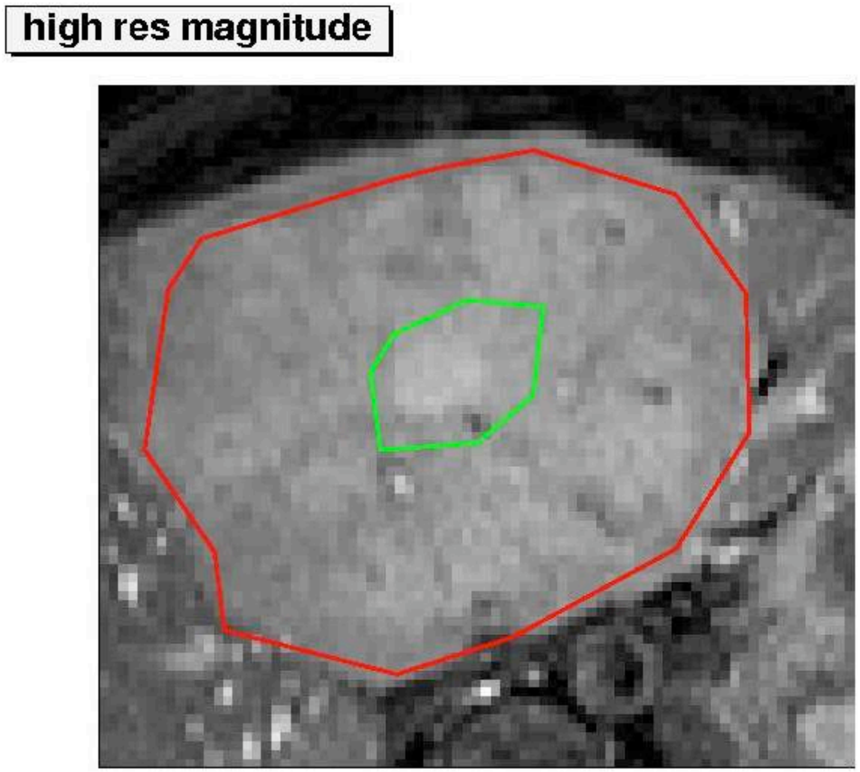


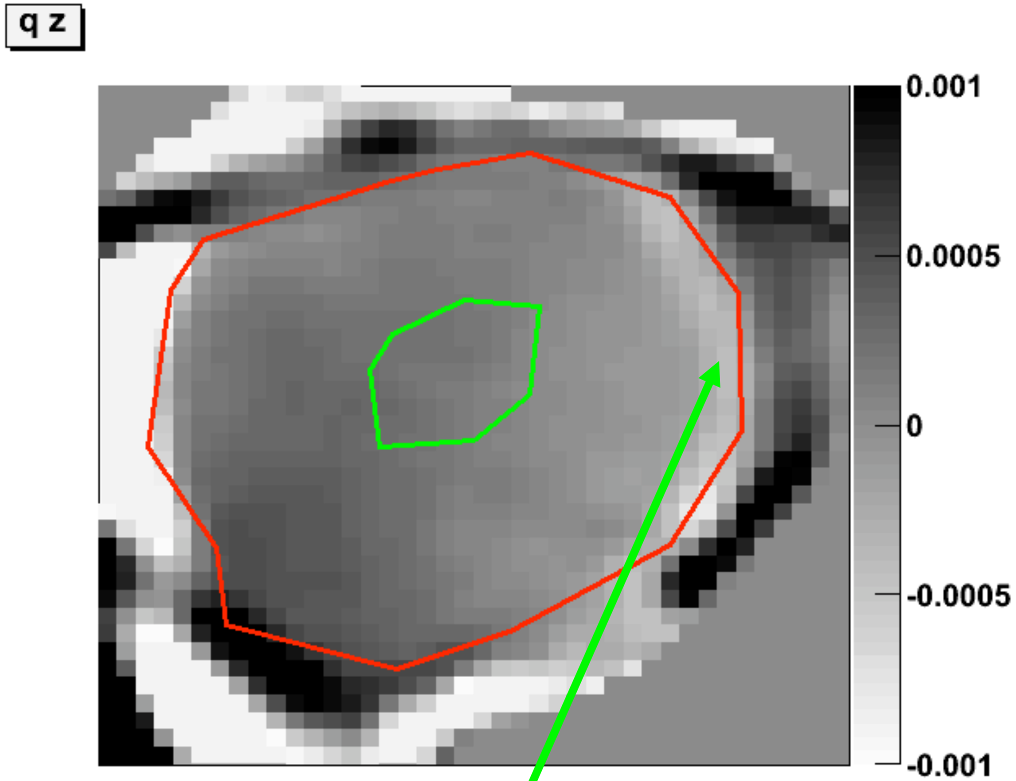


Fibrotic Cholangiocarcinoma



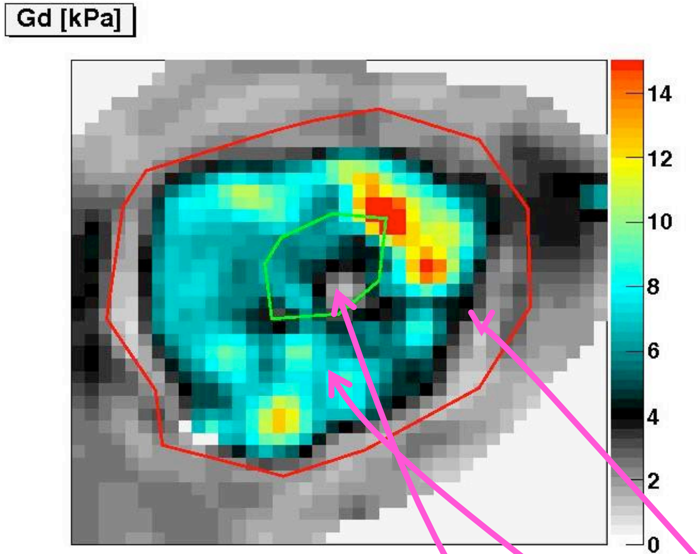
Fibrotic Cholangiocarcinoma

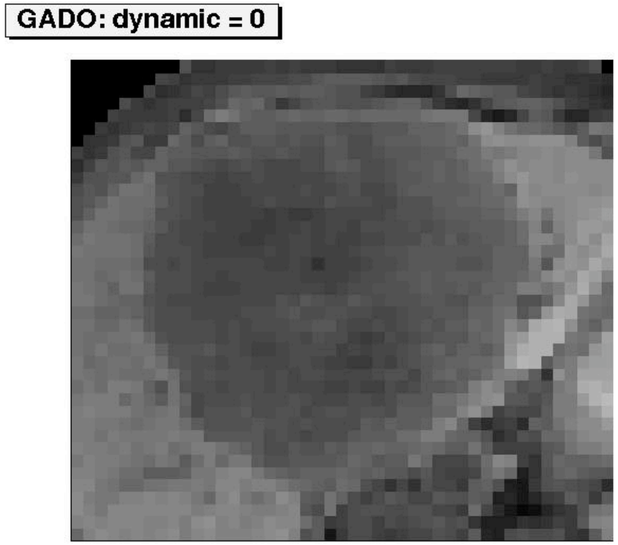


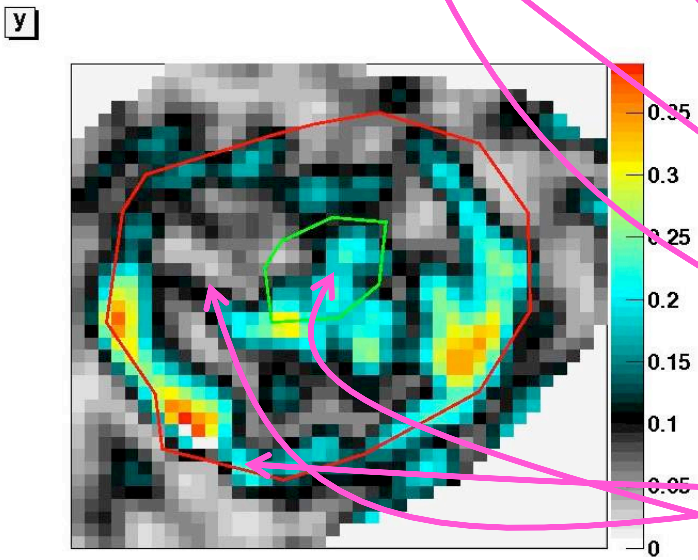


shear waves clearly enter into the lesion

Fusion with Gadolinium Data





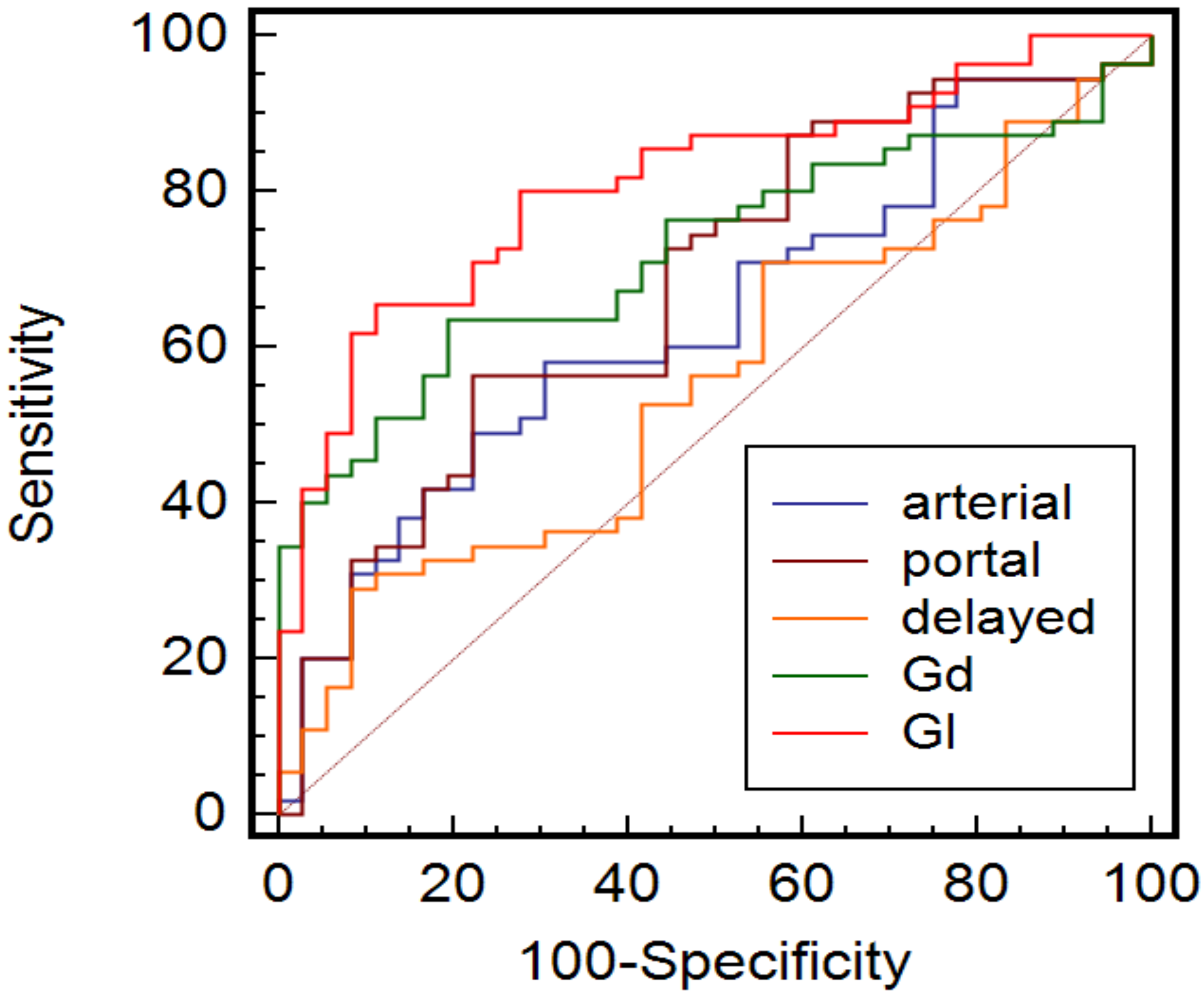


$y=1/\pi*\mathrm{atan}(Gl/Gd)$

- portal gado phase shows ring-enhancement which appears soft but strongly viscous
- fibrotic region appears very stiff but little viscous
- necrotic core appears soft and strongly viscous

Does G* provide valuable information?

First analysis from 100 tumors



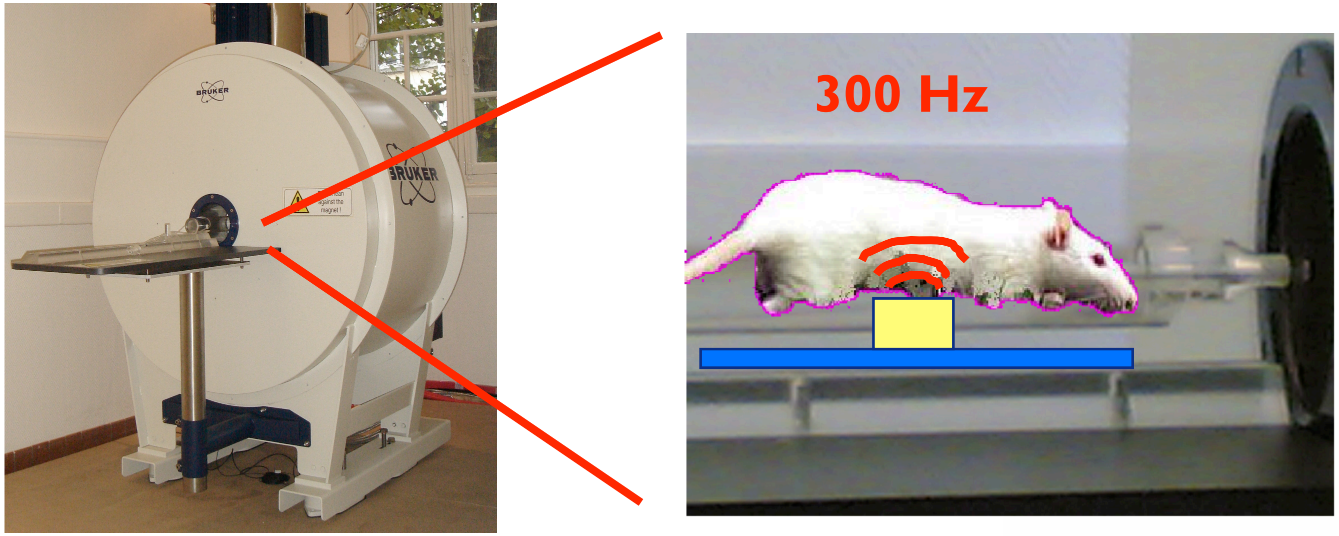
AUC values

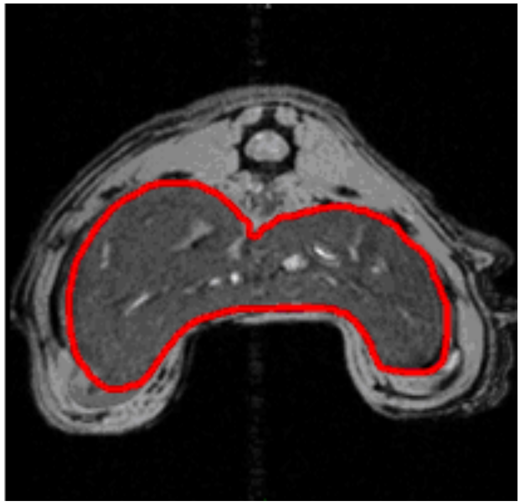
0.64 ± 0.06
0.68 ± 0.06
0.56 ± 0.06
0.72 ± 0.05
0.81 ± 0.04

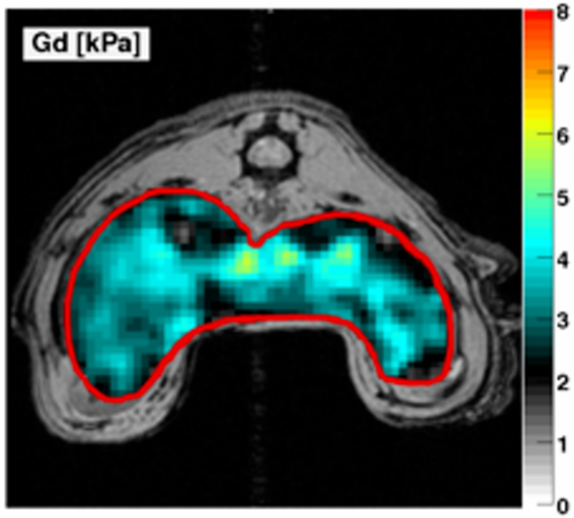
p=0.038

rat

So: is that it? Is G* the holy cow?



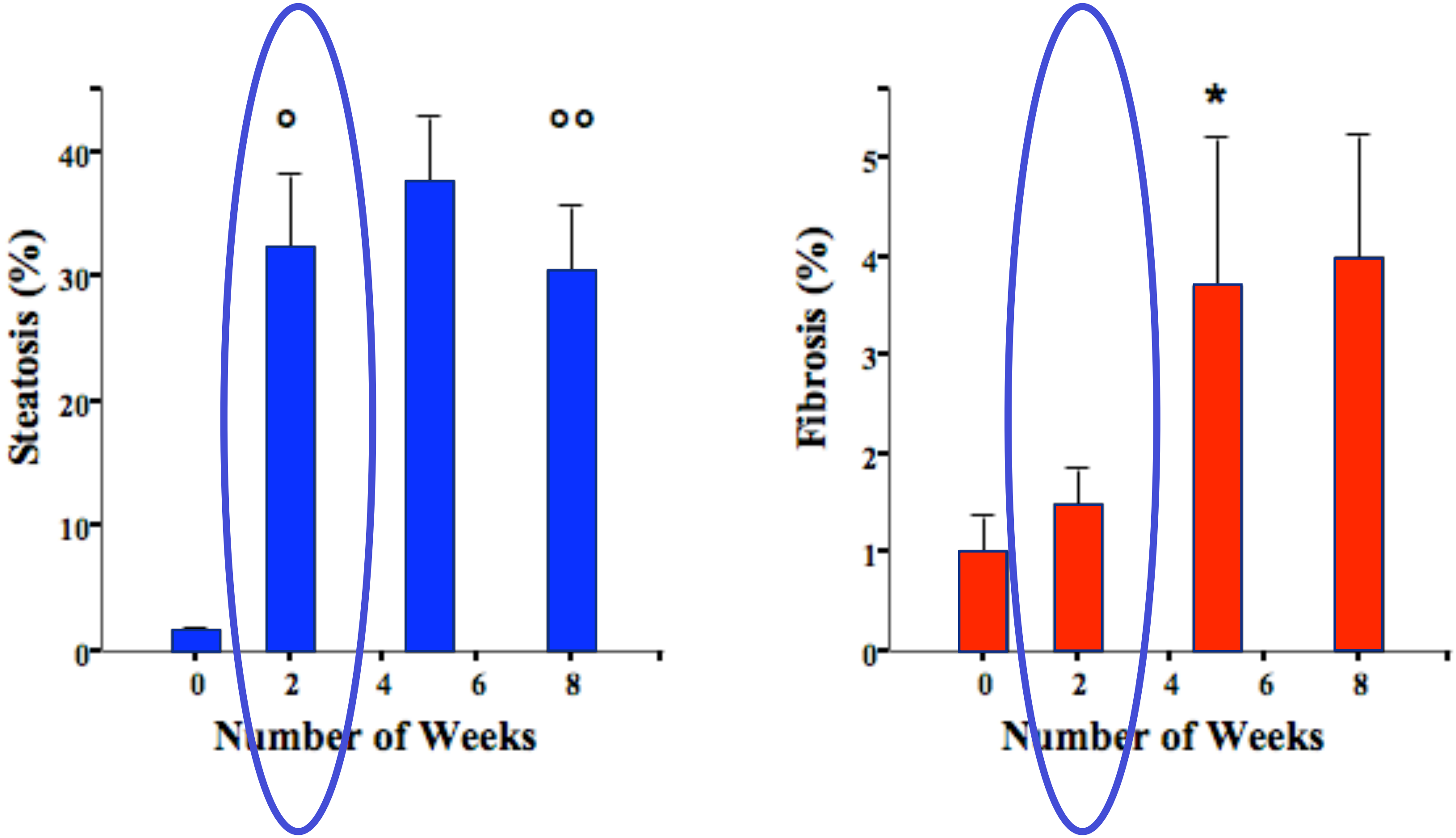




full 3D inversion

rat

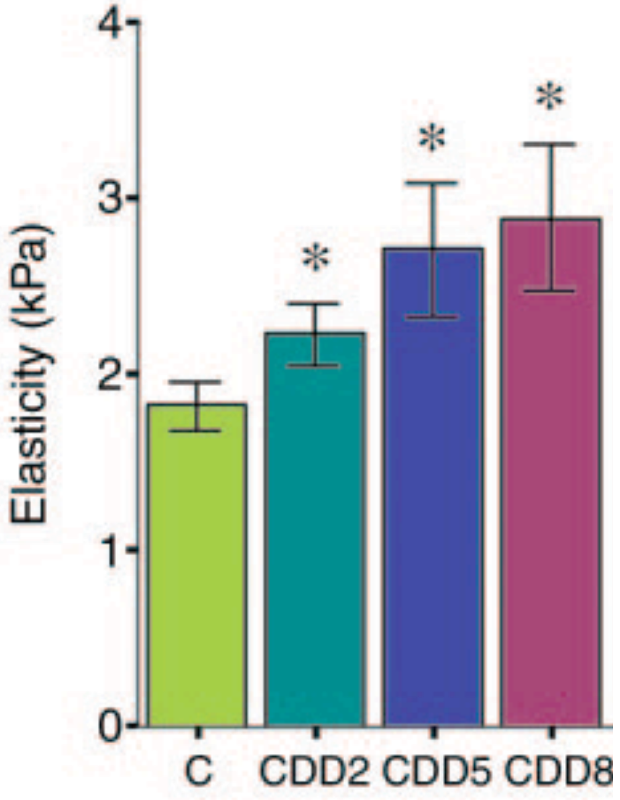
NASH: Steatosis/Fibrosis Time Course

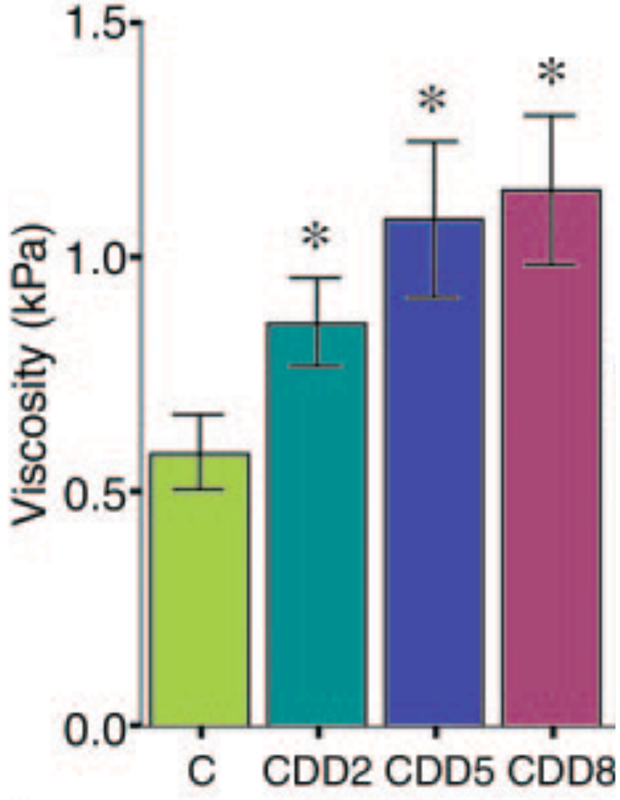


Initial steep rise of steatosis is noticeable: fibrosis follows later

rat

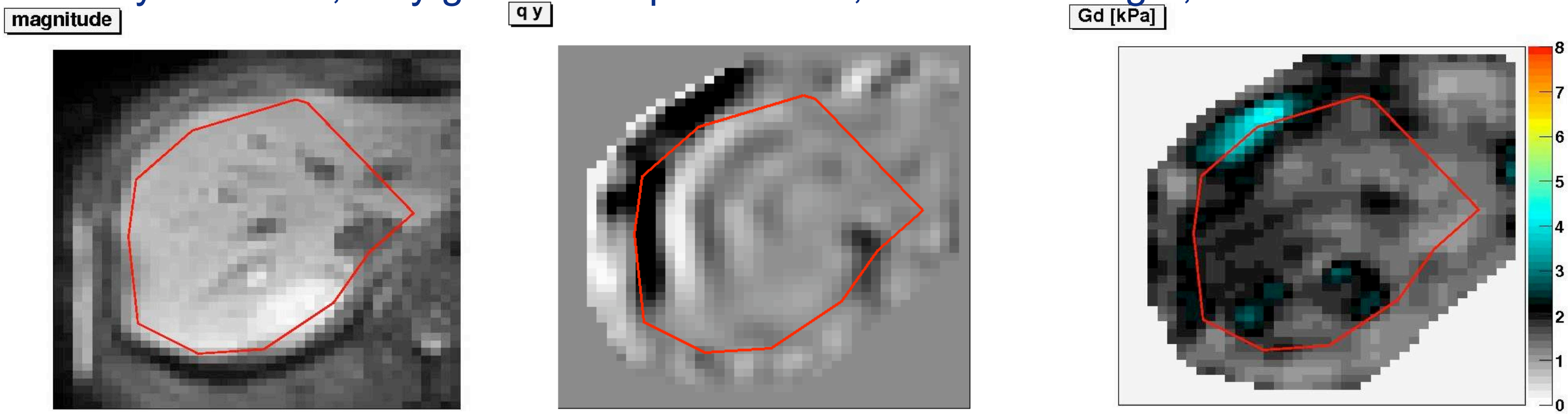
MRE Results: Elasticity & Viscosity



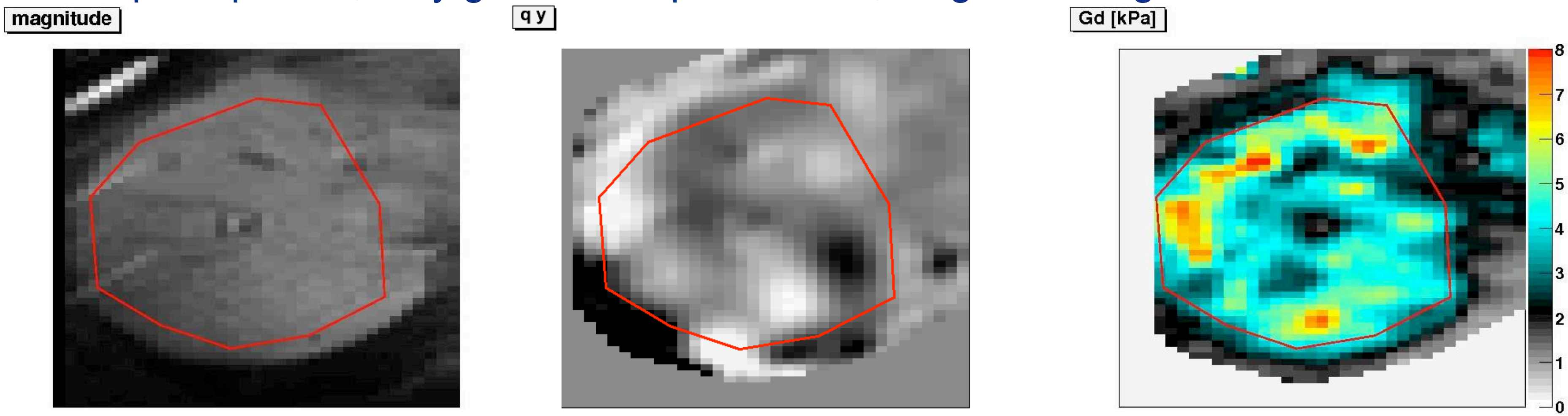


Transplant patient

Healthy volunteer, very good wave penetration, short wavelength, Gd = 1.7 ± 0.3 kPa

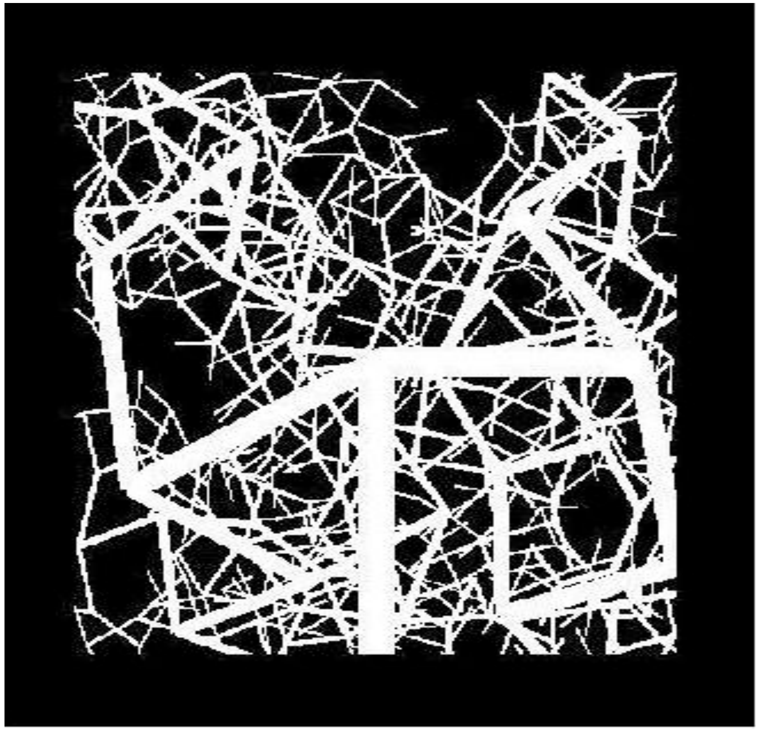


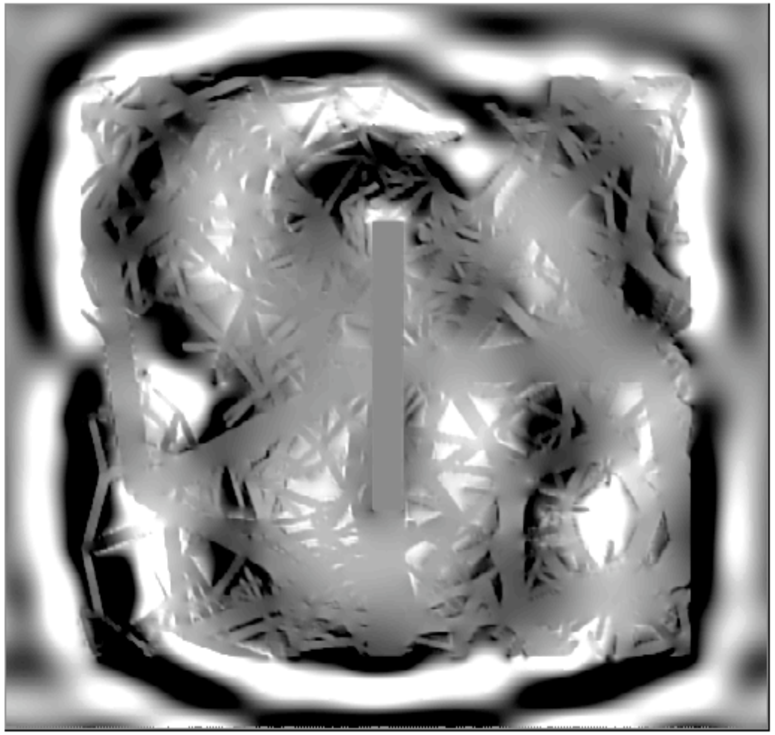
Transplant patient, very good wave penetration, long wavelength Gd = 4.0 ± 1.3 kPa



Fibroscan did not work for patient, inflammation. & light fibrosis)

Hypothesis: Presence of Vascular Tree leads to enhanced Viscosity

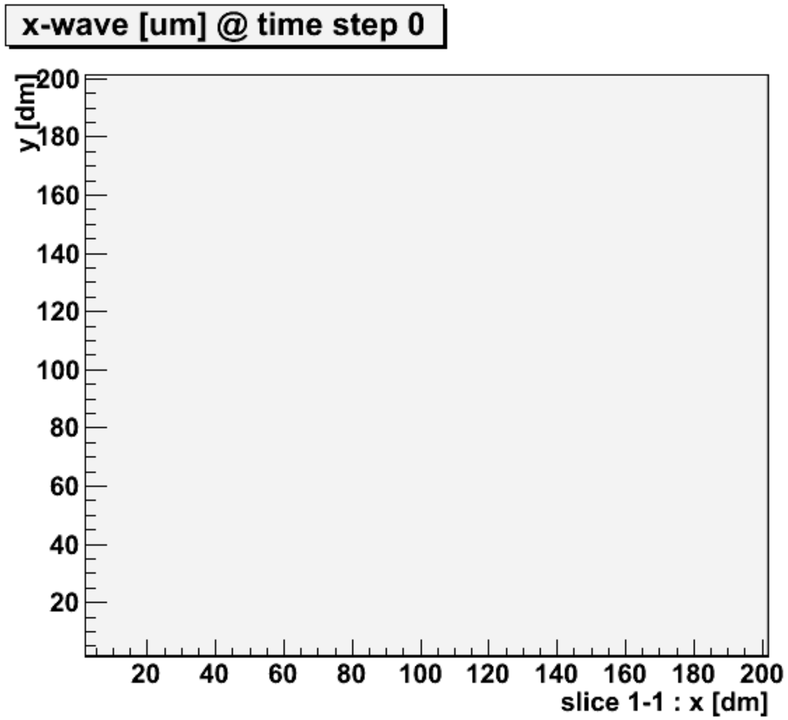




Wave Propagation in Tissue

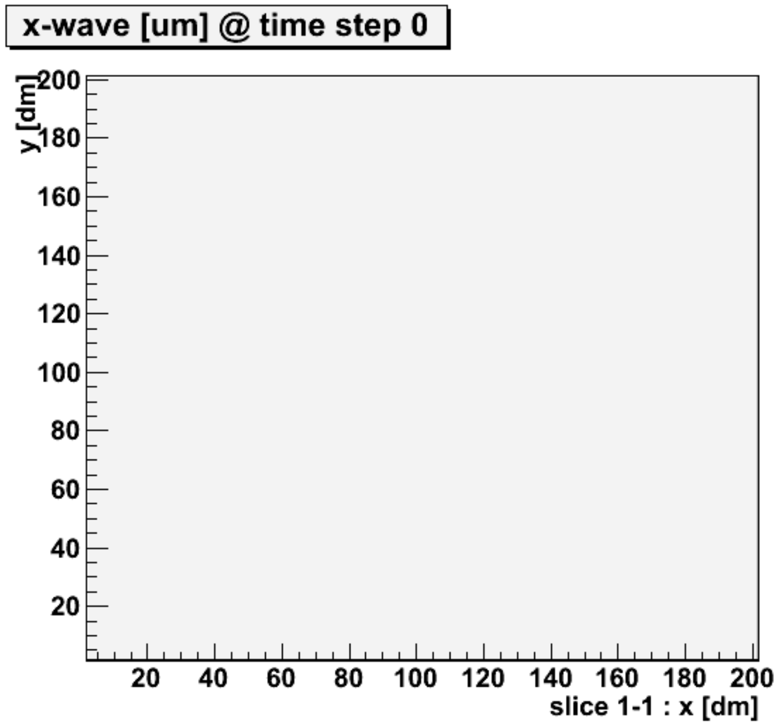
ideal world

homogeneous material

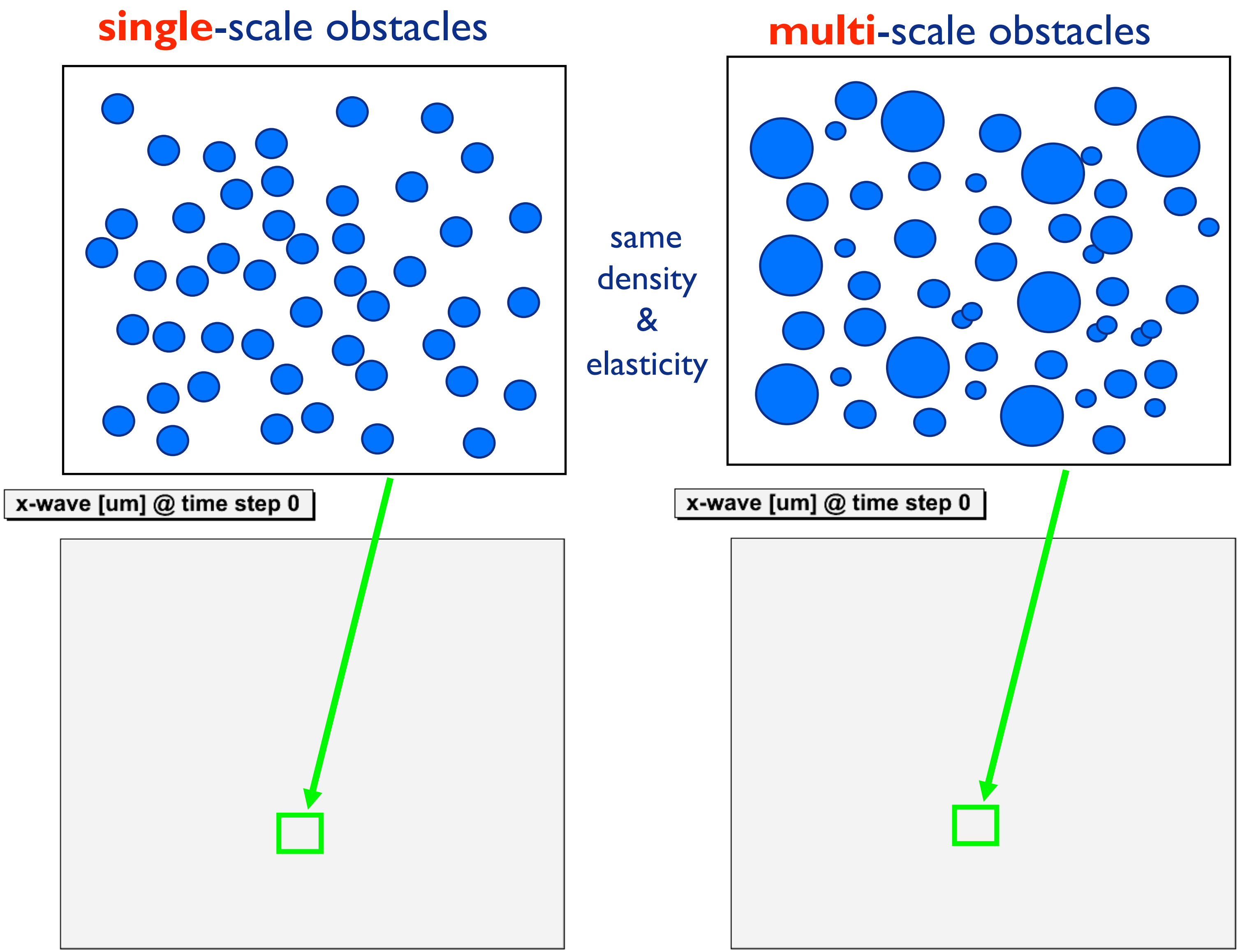


real world

heterogenous material

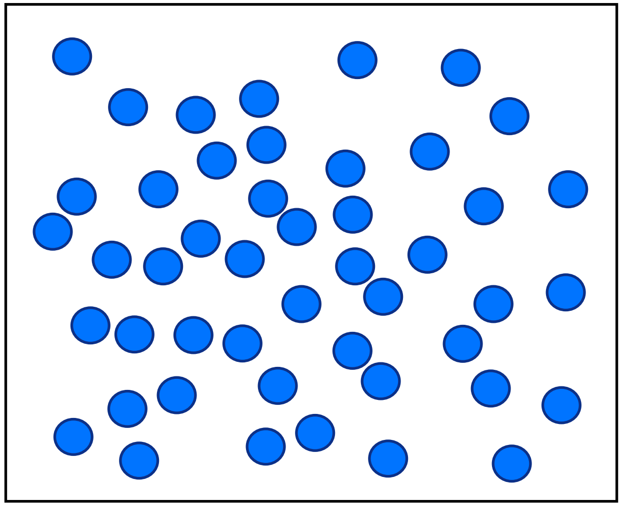


Anomalous Wave Propagation

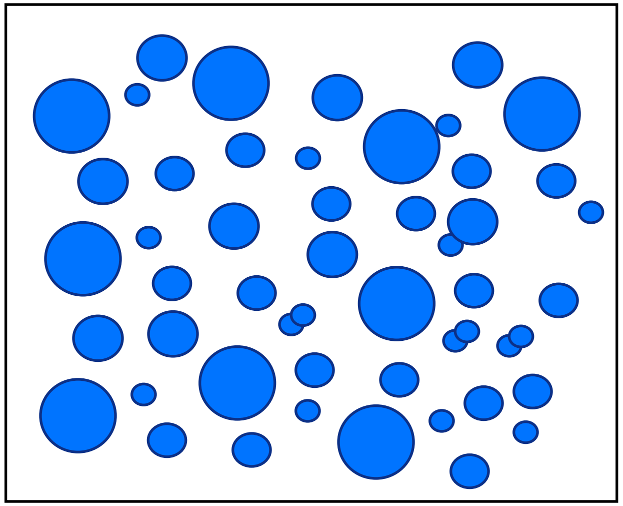


Anomalous Wave Propagation

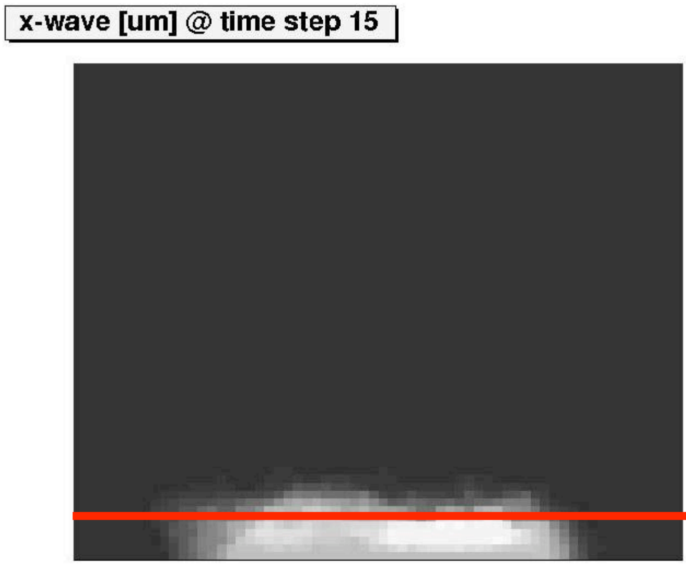
single-scale obstacles

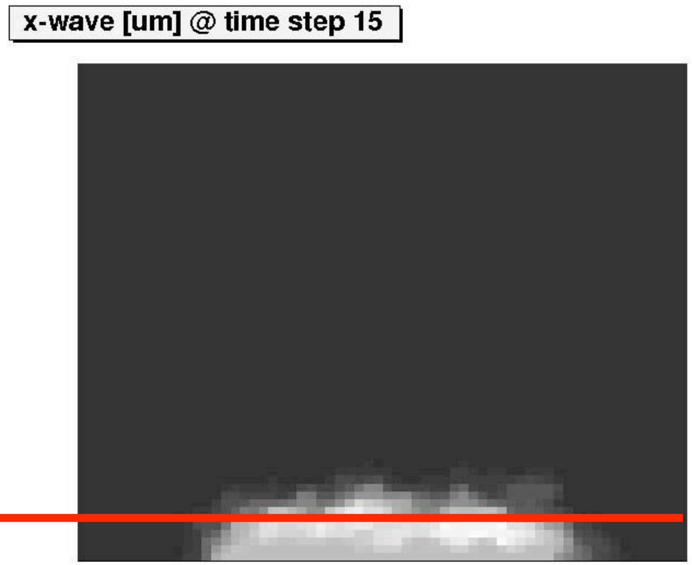


multi-scale obstacles



same density & elasticity

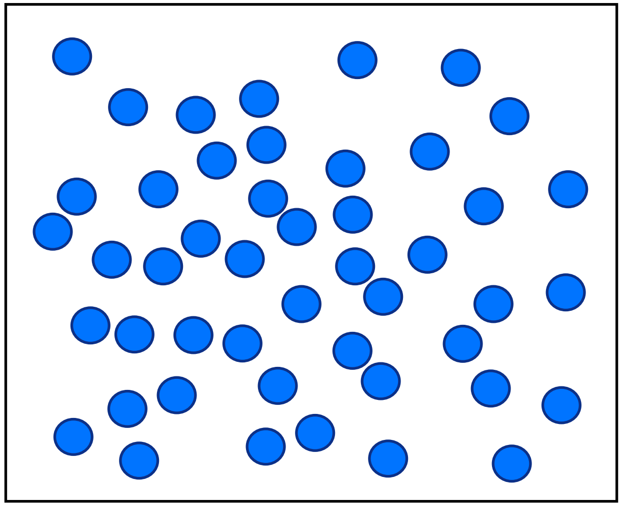




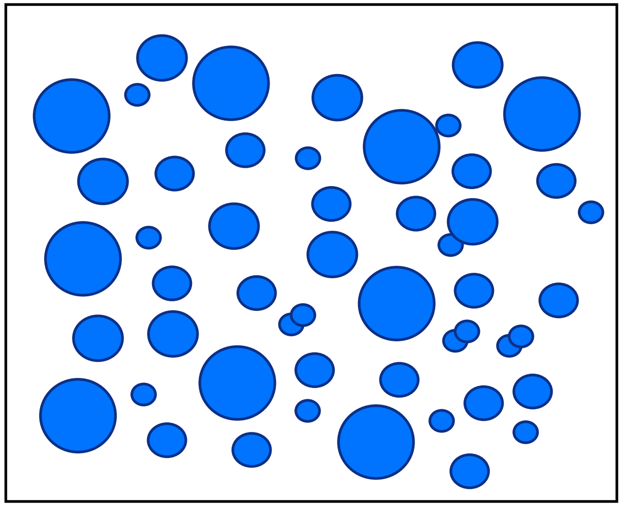
initially faster

Anomalous Wave Propagation

single-scale obstacles

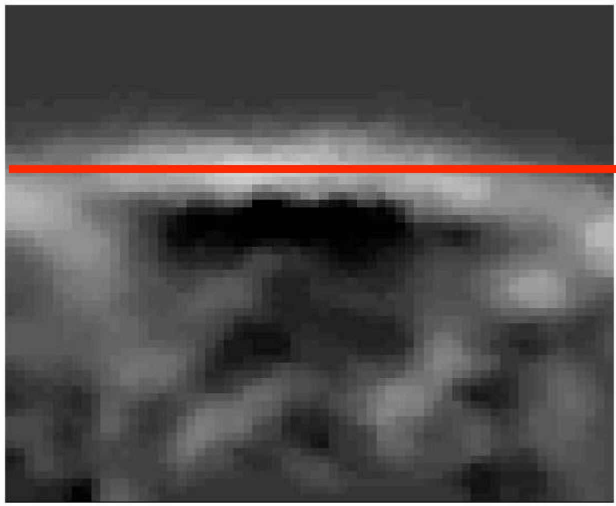


multi-scale obstacles

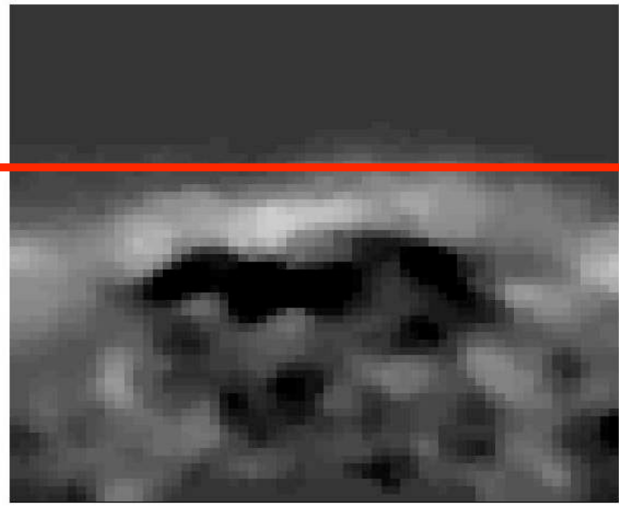


same
density
&
elasticity

x-wave [um] @ time step 79



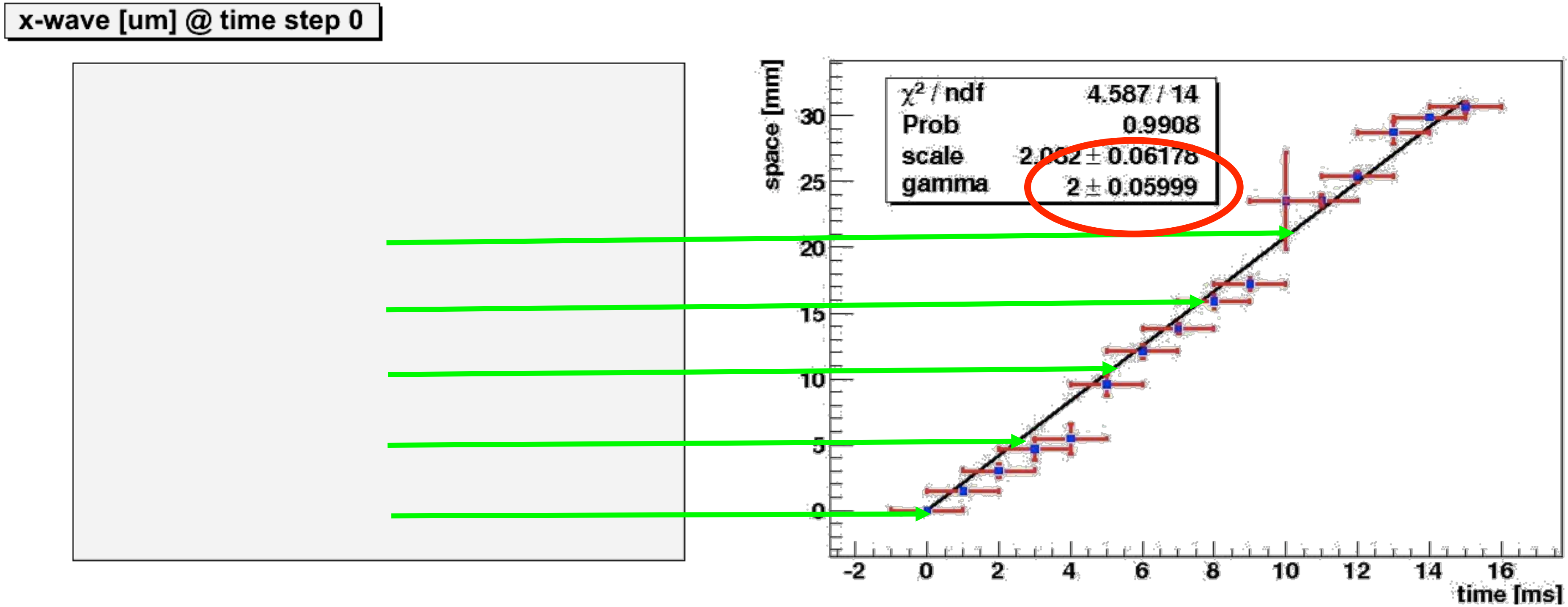
x-wave [um] @ time step 79



lags
behind

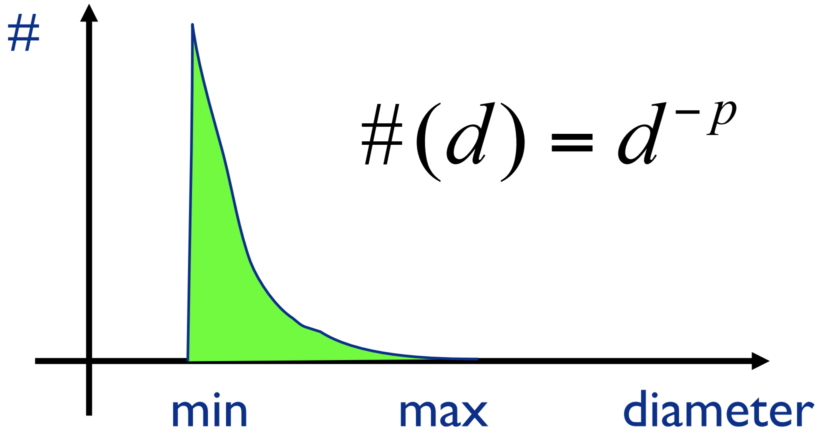
speed
changes
with time

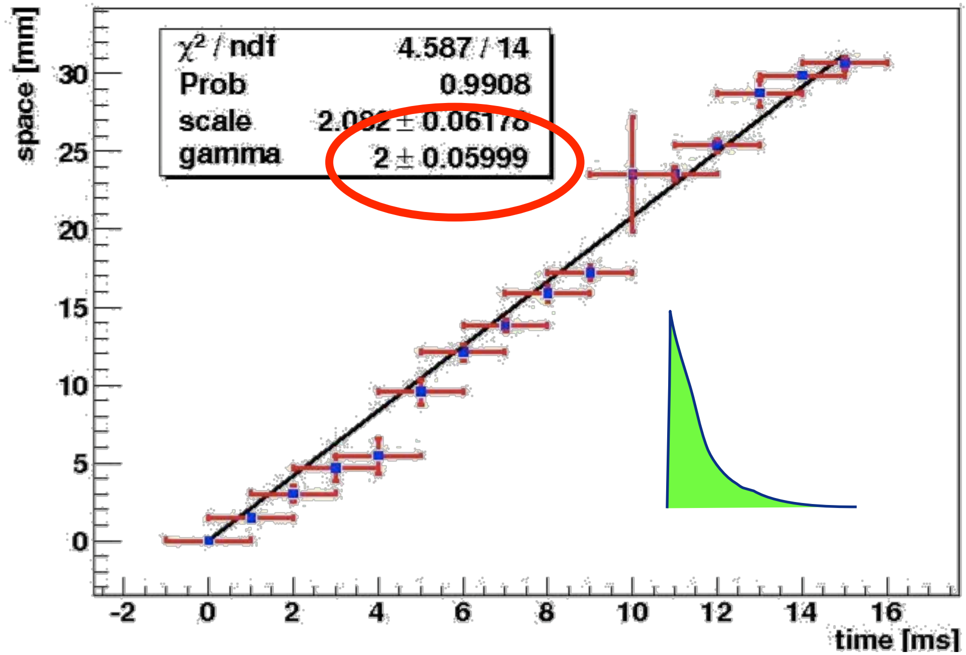
Space-Time Behavior Analysis

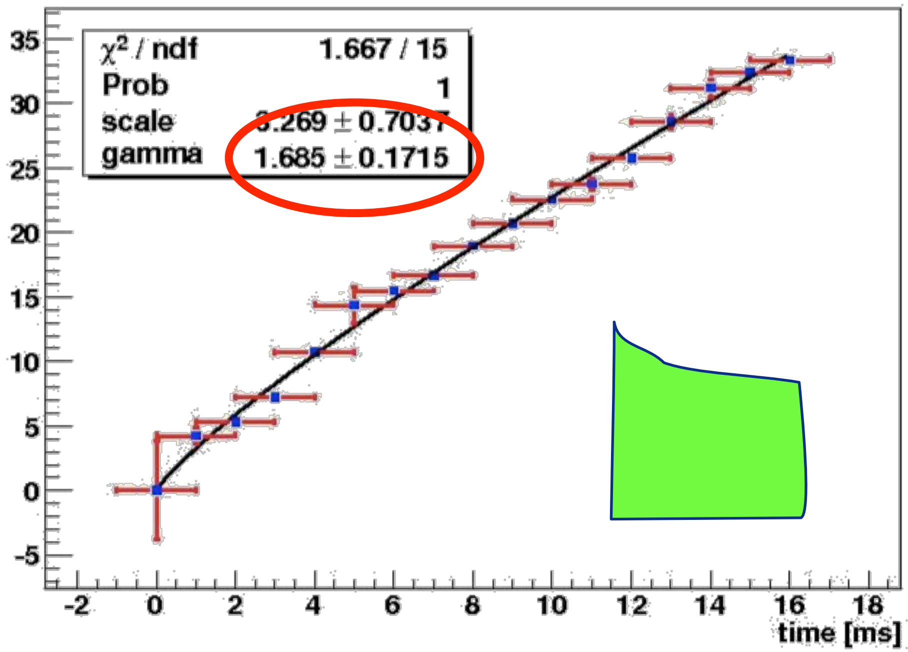


$$R(t) \sim t^{\frac{\gamma}{2}}$$

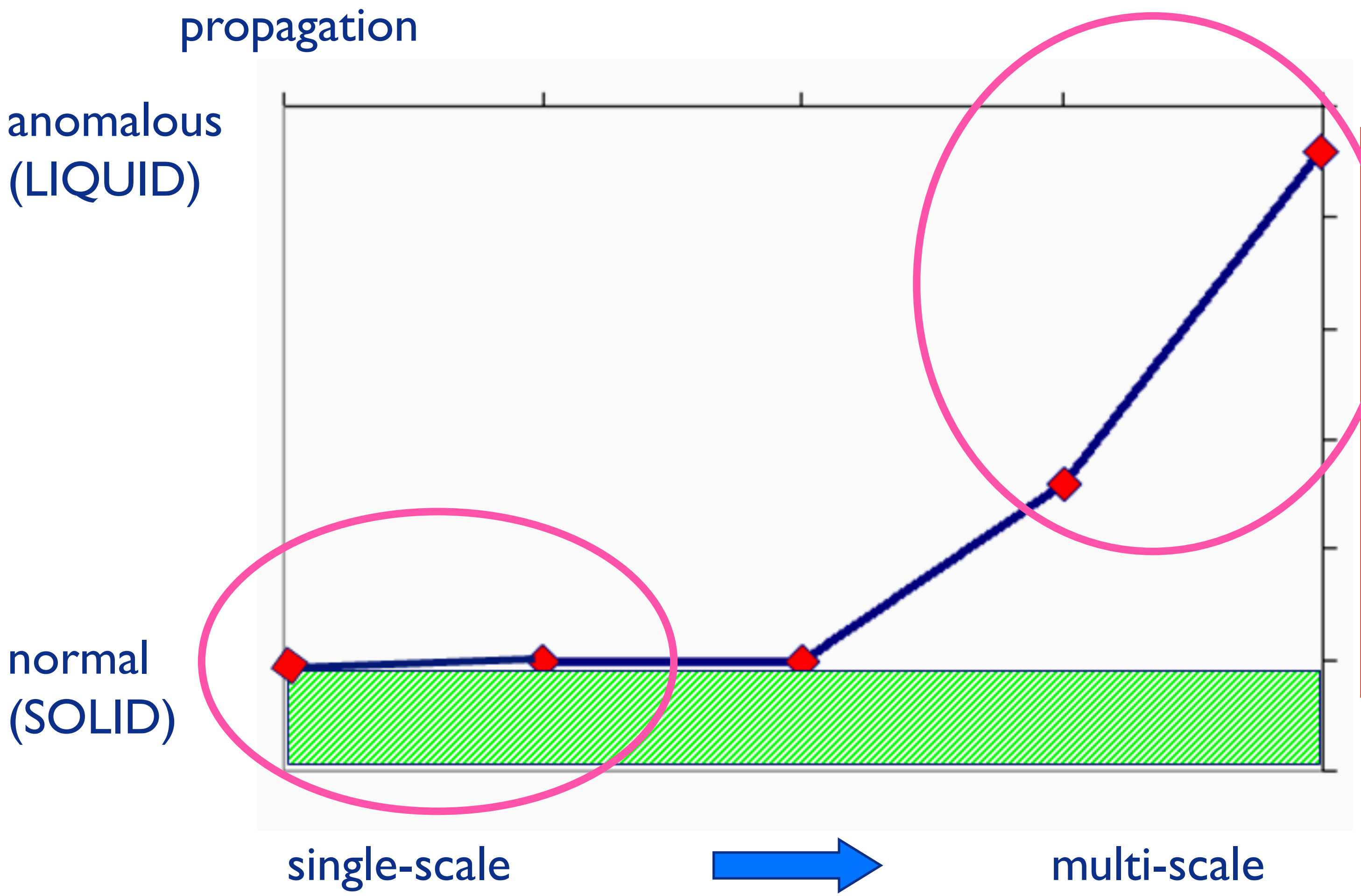
Dependency on Fractality of Obstacles







Link between Anomalous Propagation and Distribution of Obstacles



We seem to be able to assess microscopic material properties at the macroscopic scale!!!

Summary and Outlook

MRE feasible technique in clinical workflow: 1min DAQ, 3 BH

Clinical validation ongoing for liver:
fibrosis & tumors

Staging of degree of liver fibrosis in humans possible.

→ Allows non-invasive treatment follow-up

Animal models are capable to analyze influence of different pathologies (inflammation, steatosis, fibrosis)

Future: Ability to differentiate different types of fibrosis

Tumor characterization feasible and outperforms Gado info

Multi-frequency MRE will allow characterization of neo-vasculature

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