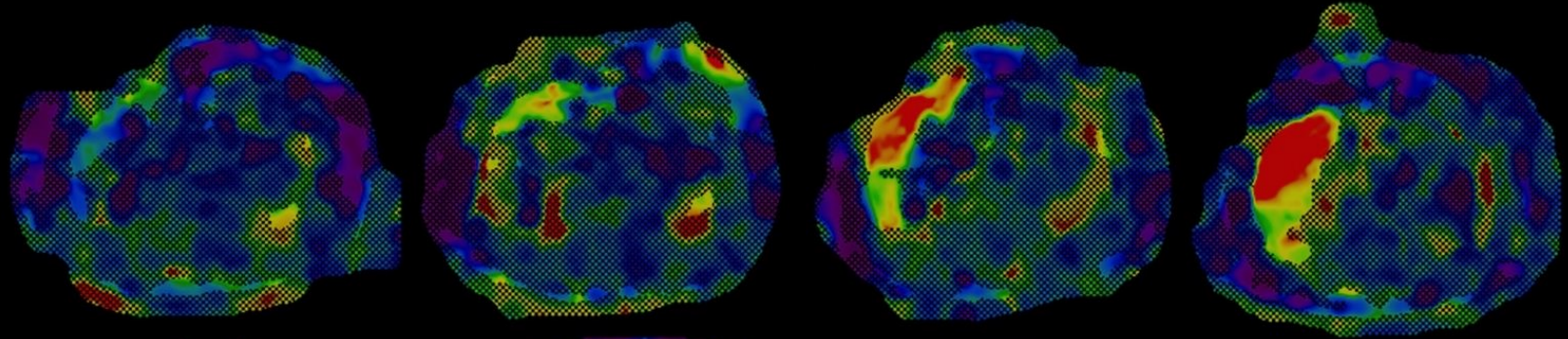
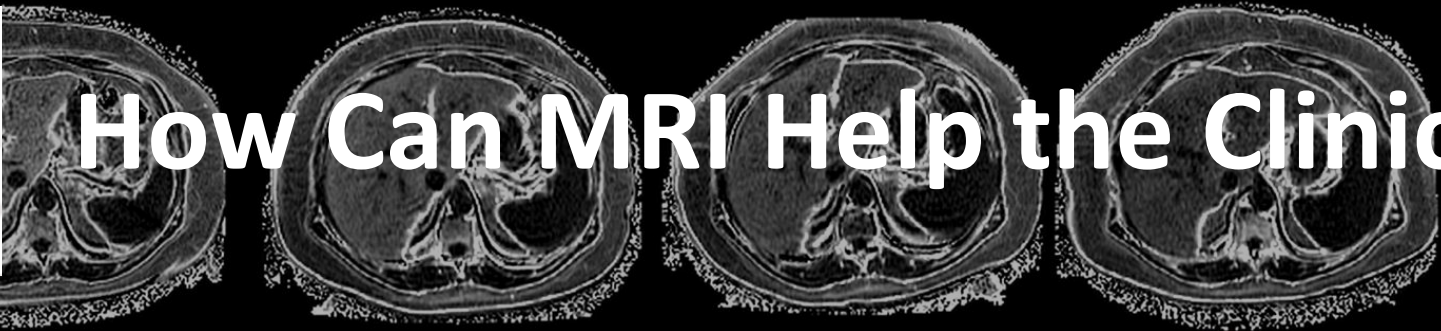


# How Can MRI Help the Clinician



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UC San Diego  
SCHOOL OF MEDICINE

# Disclosures

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## **Industry grant support**

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## **Acknowledgements**

Slides provided by Perspectum

# What Should I Talk About?

---

- Liver fat?
- Liver stiffness?
- Liver inflammation?
- Body composition?

# What Should I Talk About?

- ~~Liver fat?~~
- ~~Liver stiffness?~~
- Liver inflammation
- Body composition
- Quantitative liver function
- Mitochondrial integrity
- Oxidative stress
- Clearance functions
- Macrophage activation
- Pancreatic beta cell mass

“That’s boring”

“Talk about this”



# Goals

## What can MRI do to help the clinician

- Now
- In 5-10 years
- Pie in the Sky
- “Never”

**Focus on NAFLD/NASH diagnosis,  
prognosis, monitoring**

**HCC screening and diagnosis not  
discussed**

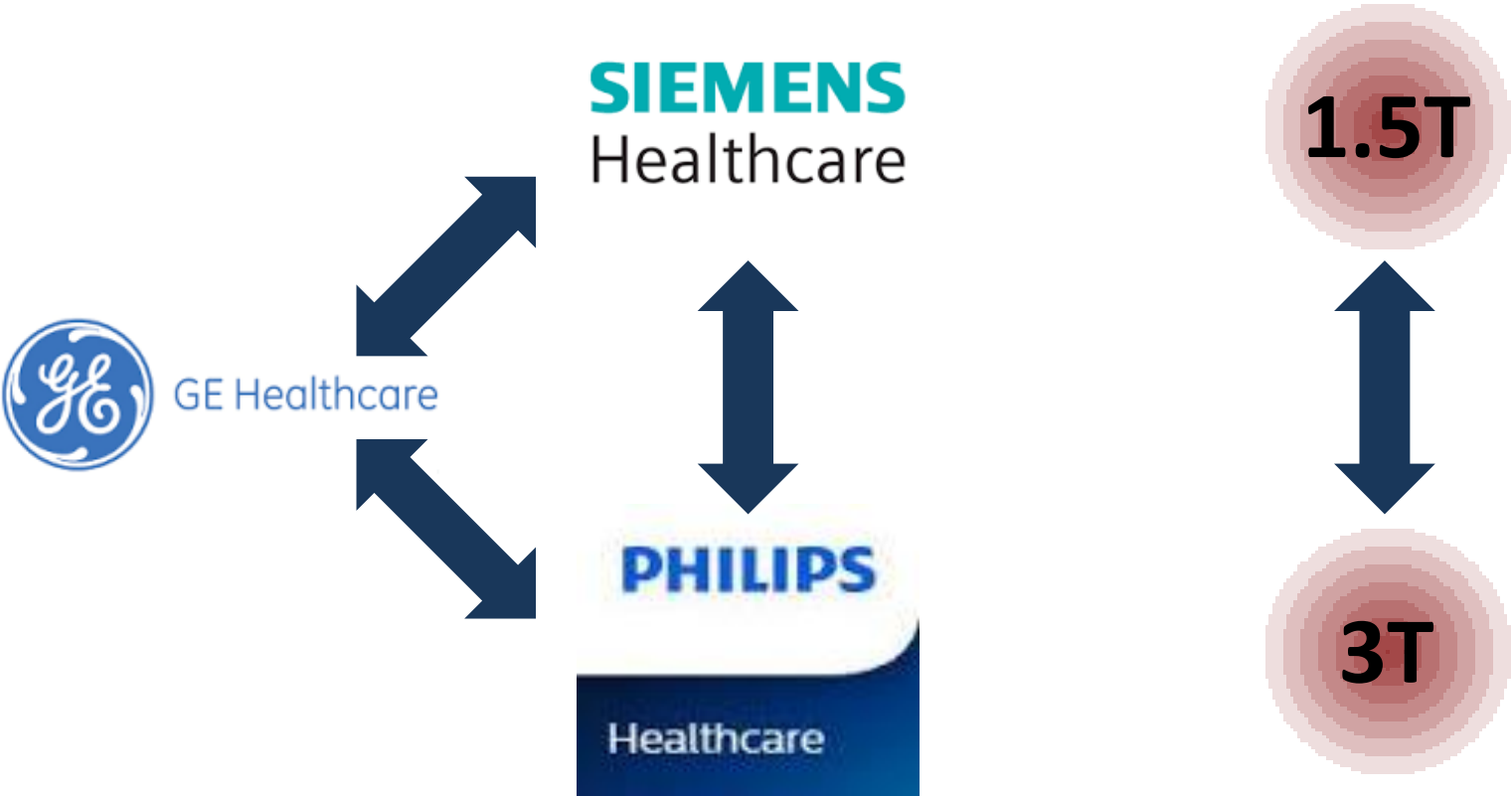
**Bridging the chasm between what is possible and  
what is wanted: some suggestions**

# Essential MRI Features

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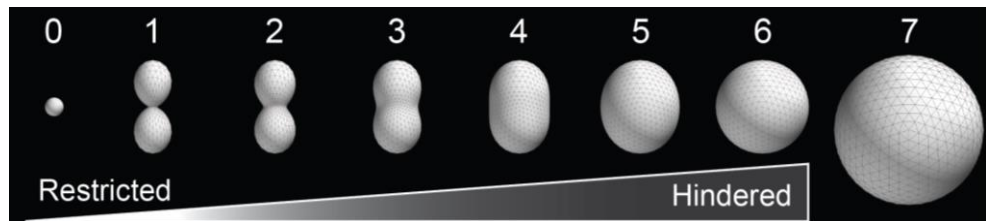
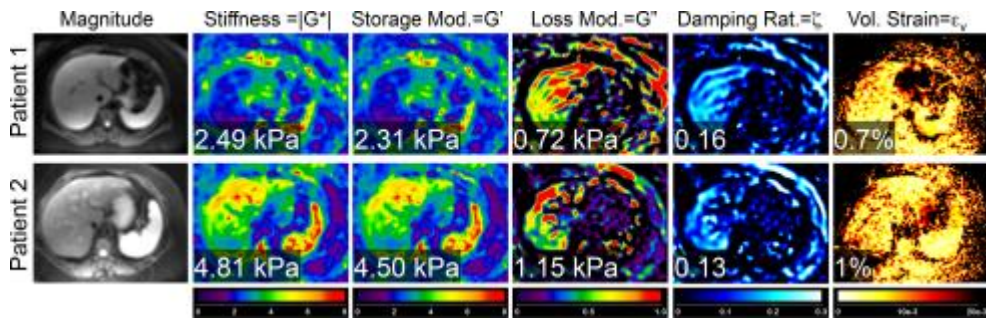
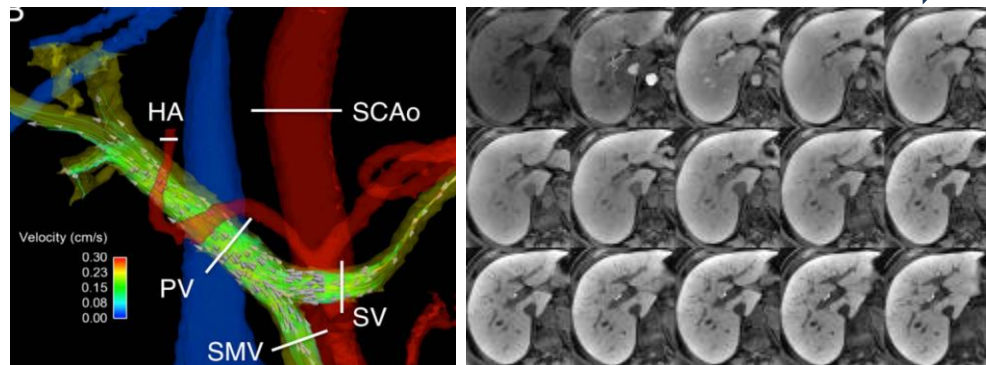
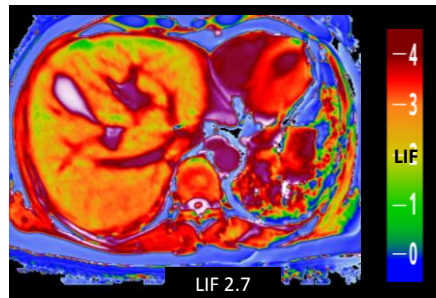
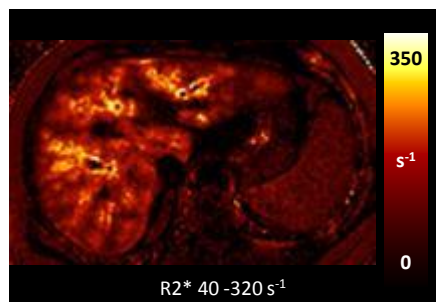
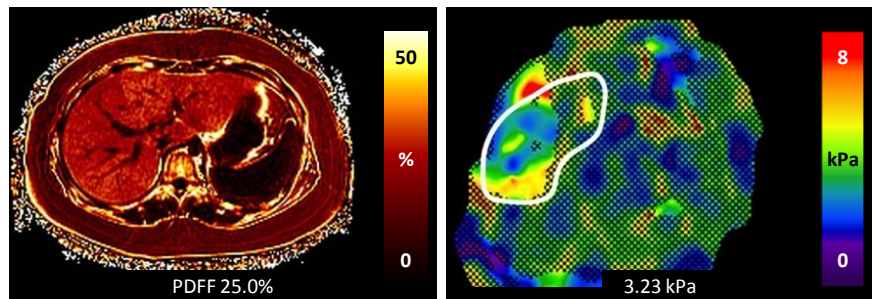
- **Available**
- **Quantitative**
- **Accurate**
- **Repeatable**
- **Reproducible**
- **Robust**
- **Practical**
- **Tolerable**
- **Affordable**
- **Meaningful**
- **Profitable**

# Available & Reproducible



# Now

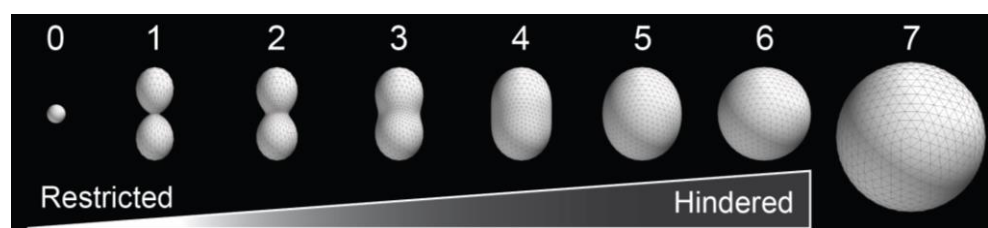
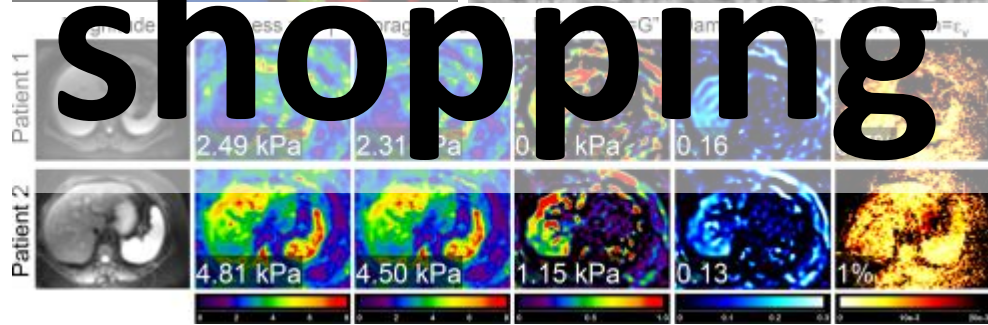
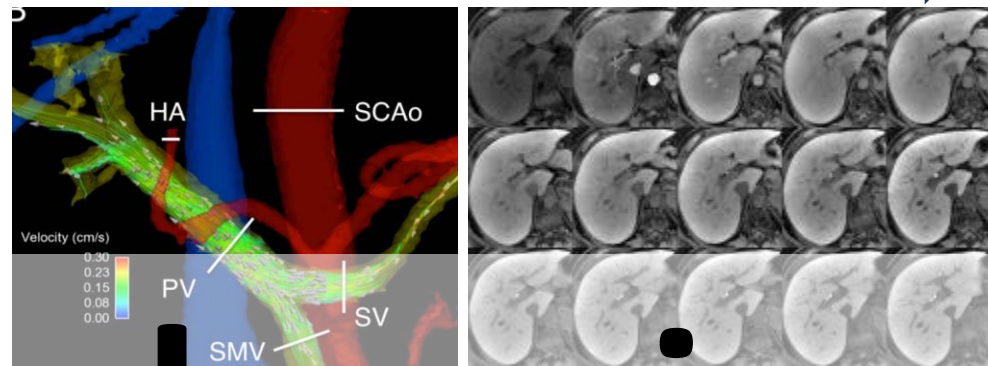
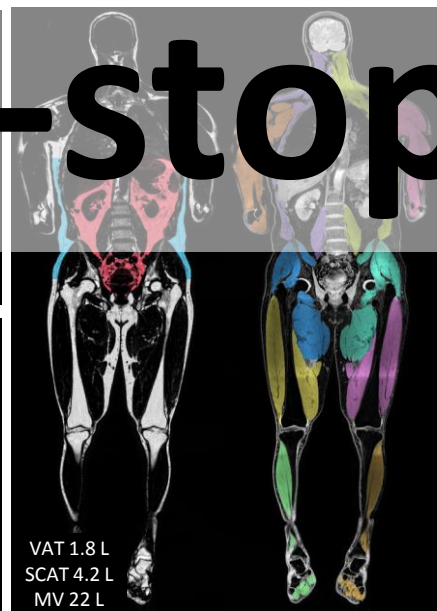
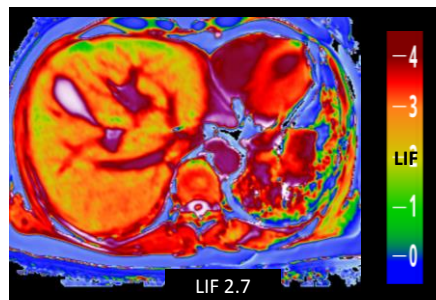
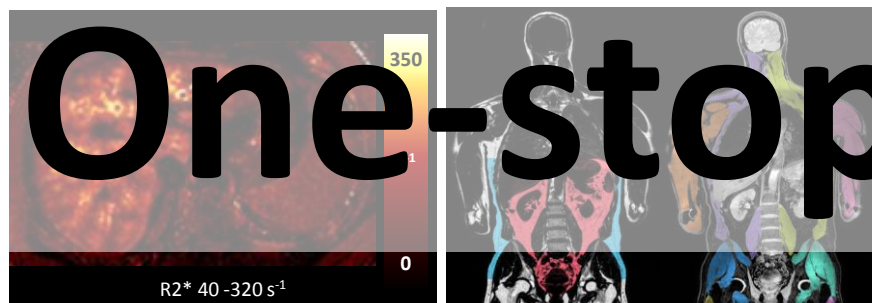
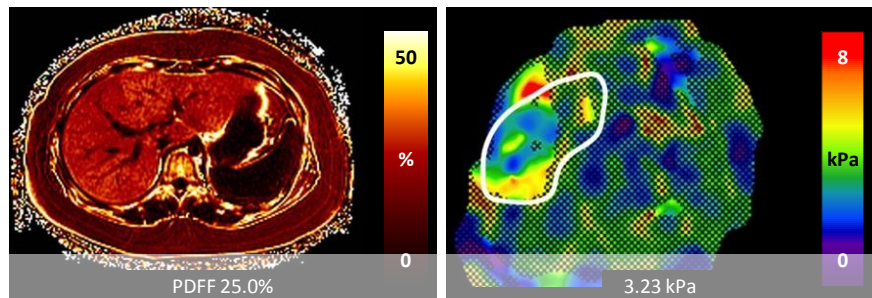
# Next 5-10 Years





Now

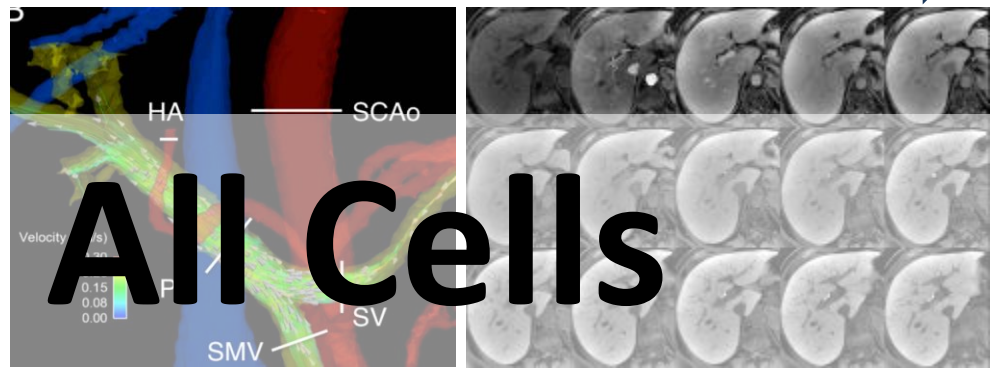
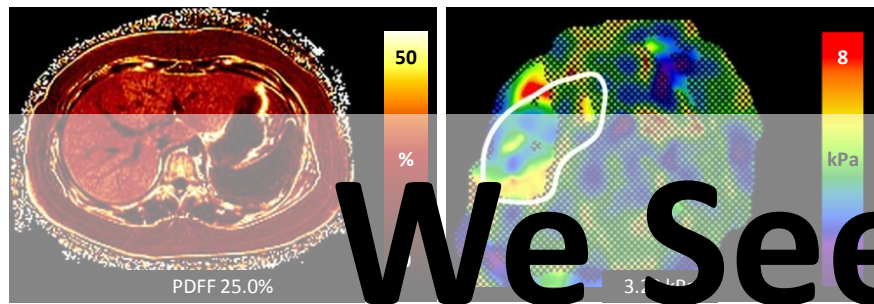
Next 5-10 Years



One-stop shopping

Now

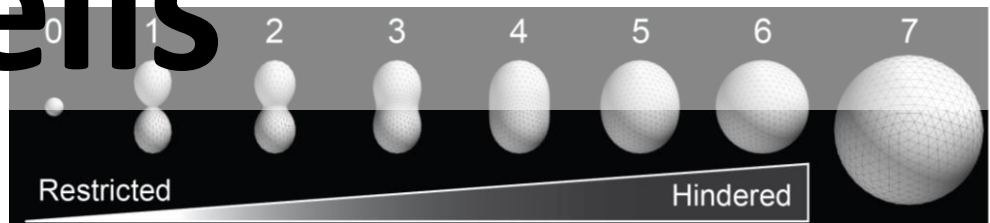
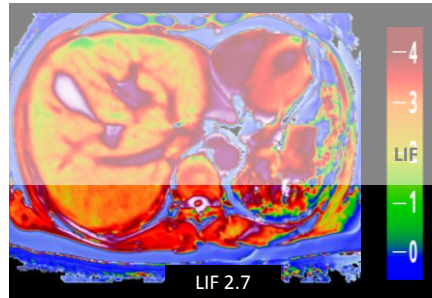
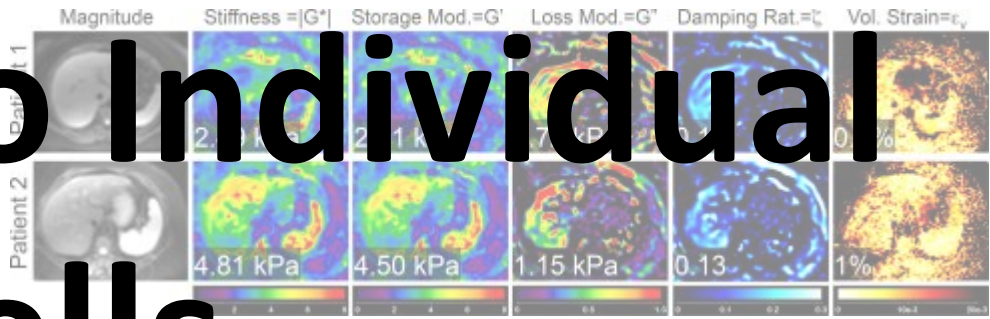
Next 5-10 Years



We See All Cells

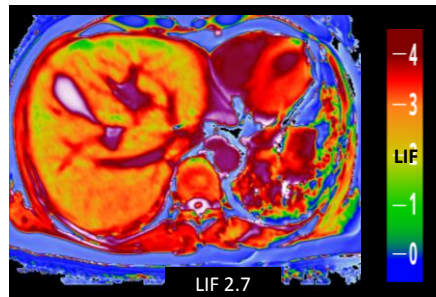
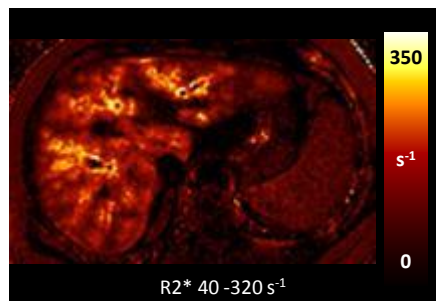
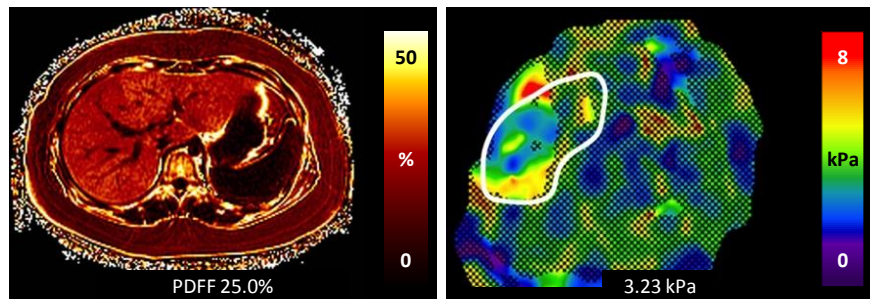


We See No Individual Cells



# Now

# Next 5-10 Years



- Refinement
- Confounder correction
- Validation
- Standardization across manufacturers
- Abbreviation
- Increasing clinical use
- Automation
- Efficiency
- Registration
- Quantitative reporting
- Big data

## Pie in the Sky

## “Never”



### Targeted contrast agents not necessary

---

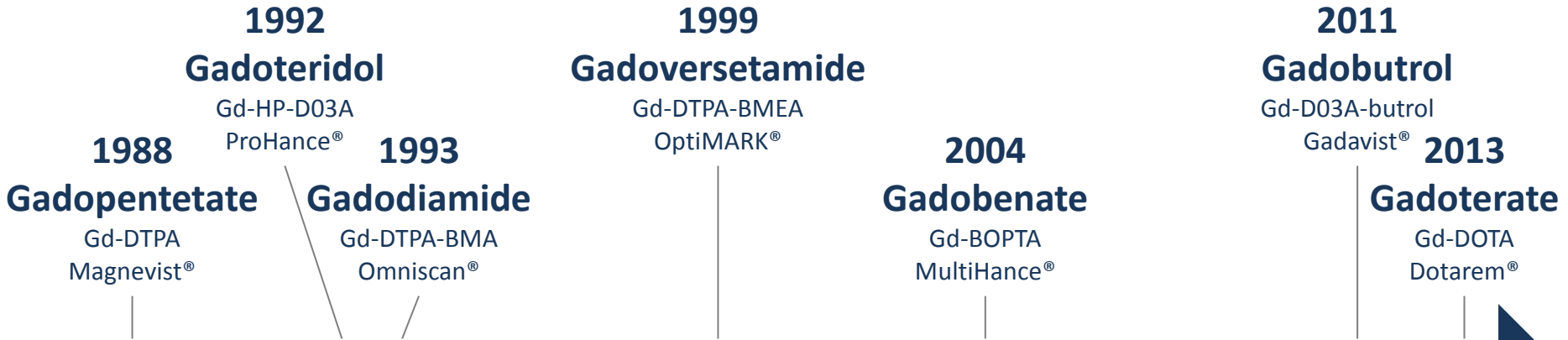
- Macromolecule content
- Triglyceride composition
- Perfusion
- Oxygenation
- Temperature

### Targeted contrast agents necessary

---

- Collagen content
- Fibrogenesis, fibrolysis
- Stellate cell activation
- Mitochondrial integrity
- Oxidative stress
- Immune activation
- Pancreatic beta cell mass

# General-use agents



11 MRI Contrast Agents Approved for Use in U.S.A.

# Specific-use agents



**Dose of Gx = US\$ 135**

Individual patients:  $\leq 4$  doses/year

**Profit threshold**

$\sim 1.5$  million doses worldwide/year

**Leading general-use MRI agent**

$\sim 10$  million doses/year



**16 years,  $\sim$  US\$ 200 million**

**1992**

**First publication on gadoxetate**

Gabriele Schuhmann-Giampieri, PhD • Heribert Schmitt-Willich, PhD • Wolf-Rüdiger Press  
Chikashi Negishi, MD • Hanns-Joachim Weinmann, PhD • Ulrich Speck, PhD

**Preclinical Evaluation of Gd-EOB-DTPA  
as a Contrast Agent in MR Imaging  
of the Hepatobiliary System<sup>1</sup>**

**2008**

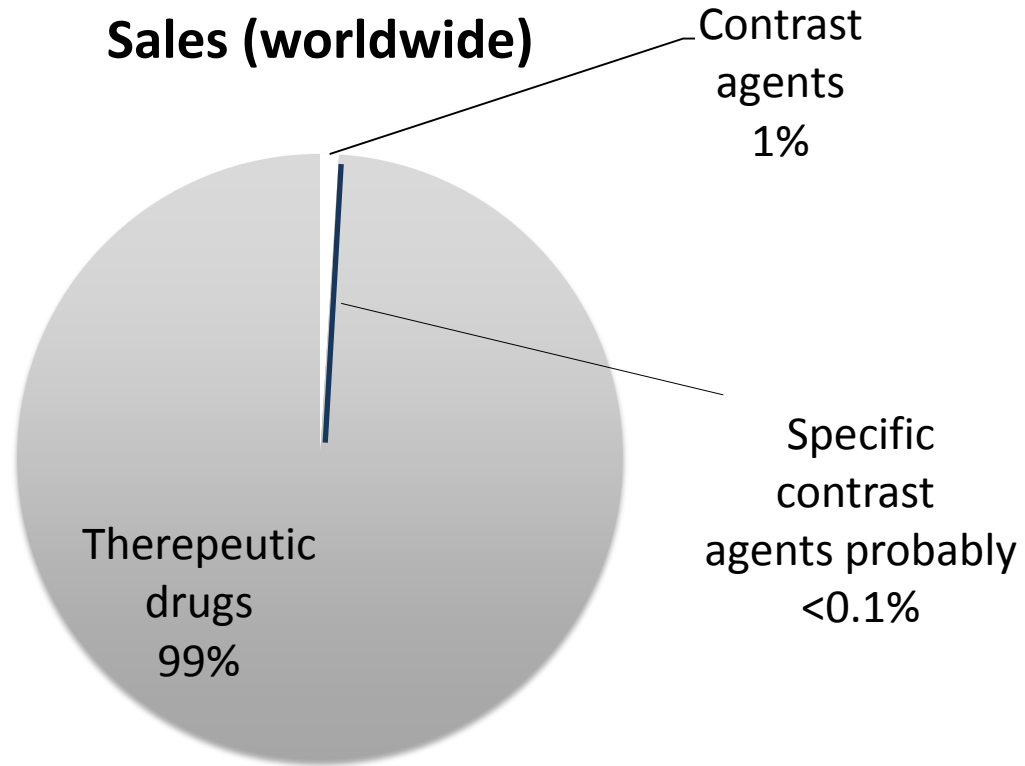
**Gadoxetate**

Gd-EOB-DTPA

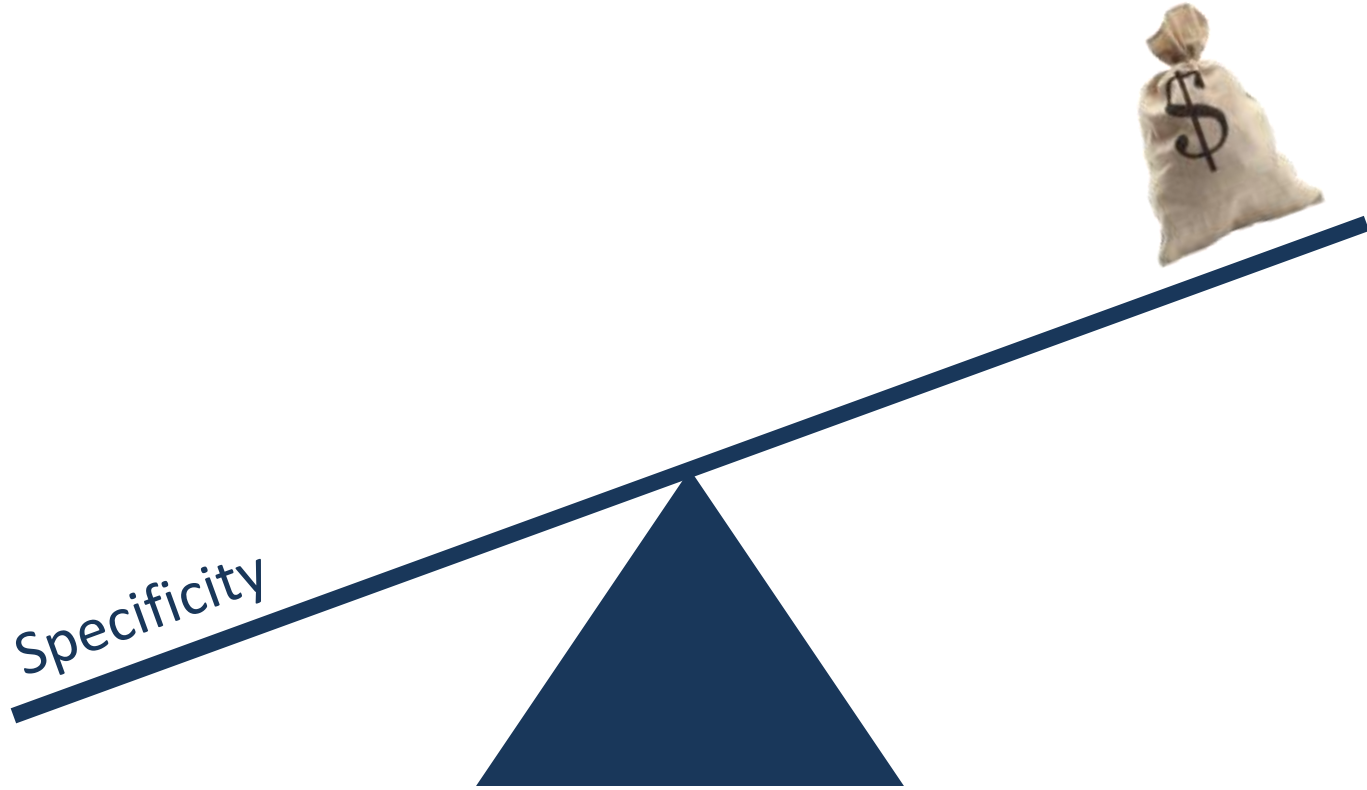
Primovist®

Eovist®

# All Radiology Contrast Agents – Global Sales



# Contrast Agent Development: A Tradeoff





# The Chasm



## What is Possible (Now or Eventually)

---

- PDFF
- Stiffness, other mech. properties
- R2, R2\*
- Iron-corrected T1
- Body composition
- Blood flow
- Advanced diffusion
- Quantitative OATP/MRP function
- Macromolecule content
- Triglyceride composition
- Perfusion, oxygenation, temperature

## What is Wanted

---

- Collagen content
- Fibrogenesis
- Fibrolysis
- Stellate cell activation
- Mitochondrial integrity
- Oxidative stress
- Immune activation
- Pancreatic beta cell mass

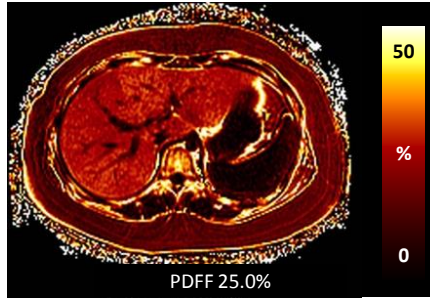
# Bridging the Chasm

A suspension bridge with wooden planks and metal cables spans a deep, dark chasm. The background features jagged, dark rock formations under a clear blue sky. The bridge's cables and railings are visible in the foreground, leading the eye towards the center of the chasm.

- **Paradigm shift**
- **Multidisciplinary imaging biomarker consortium**

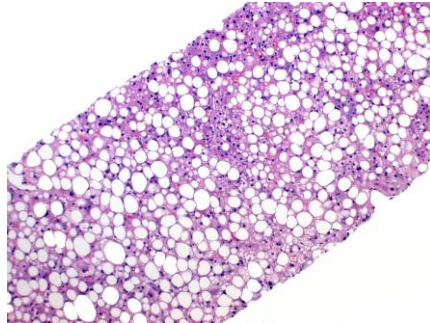
# Current Paradigm

Chemical Shift MRI

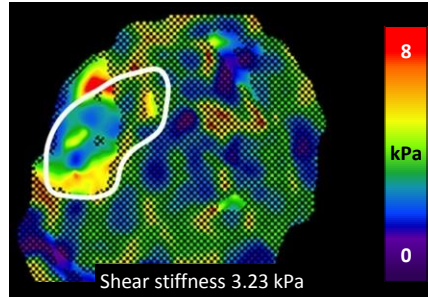


PDFF

Steatosis

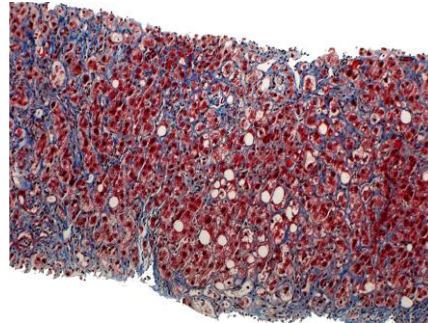


MRE

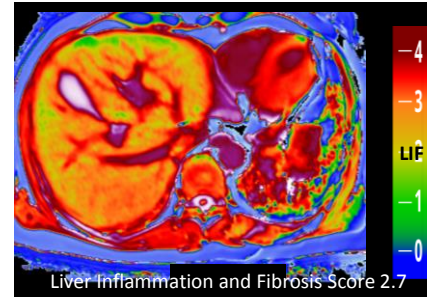


Shear stiffness

Fibrosis

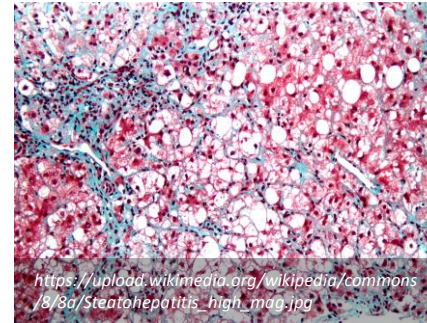


Liver MultiScan



Corrected T1

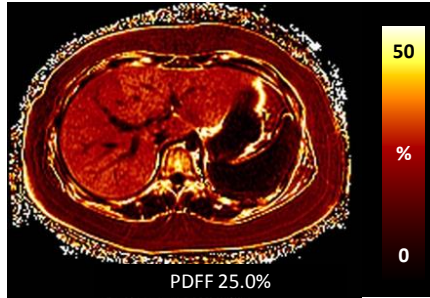
Inflammation and Fibrosis



- MRI measurements no intrinsic meaning
- Must be translated into a histology score

# New Paradigm

Chemical Shift MRI

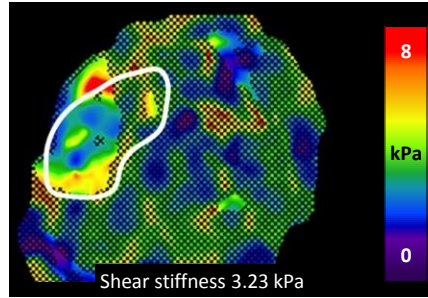


PDFF

[Triglyceride]  
within

MRI visible protons

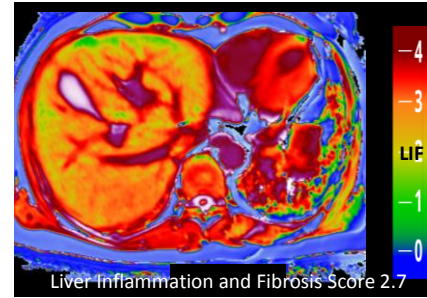
MRE



Shear stiffness

Elastic and viscous  
components of  
shear stiffness

Liver MultiScan



Corrected T1

Water content  
within  
MRI visible protons

Outcomes

- MRI measurements acquire intrinsic meaning
- Do not have to be translated into a histology score

# Multi-Disciplinary Imaging Biomarker Consortium

- Academia, industry, agencies
- Hepatology, pathology, radiology, molecular biology, physics, computer science and engineering
- Understand needs, capabilities, challenges, limitations
- Important but realistic goals
- Methods that don't require specific contrast agents
- Identify suitable targets to develop specific agents with potentially sustainable economic markets

# Never Say Never



## **Charles Holland Duell**

Commissioner of the United States Patent and Trademark Office  
1898 -1901

### **Apocryphal quote:**

“Everything that can be invented has been invented.”

### **Actual quote:**

“All previous advances in the various lines of invention will appear totally insignificant when compared with those which the present century will witness. I almost wish that I might live my life over again to see the wonders which are at the threshold.”