ADVANCED CARDIAC MRI
A TECHNICAL OVERVIEW

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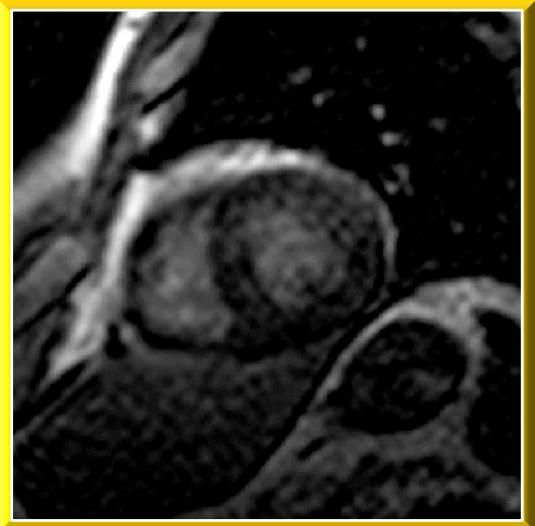
CIBM

UNIL | Université de Lausanne
Radiodiagnostic et radiologie interventionnelle

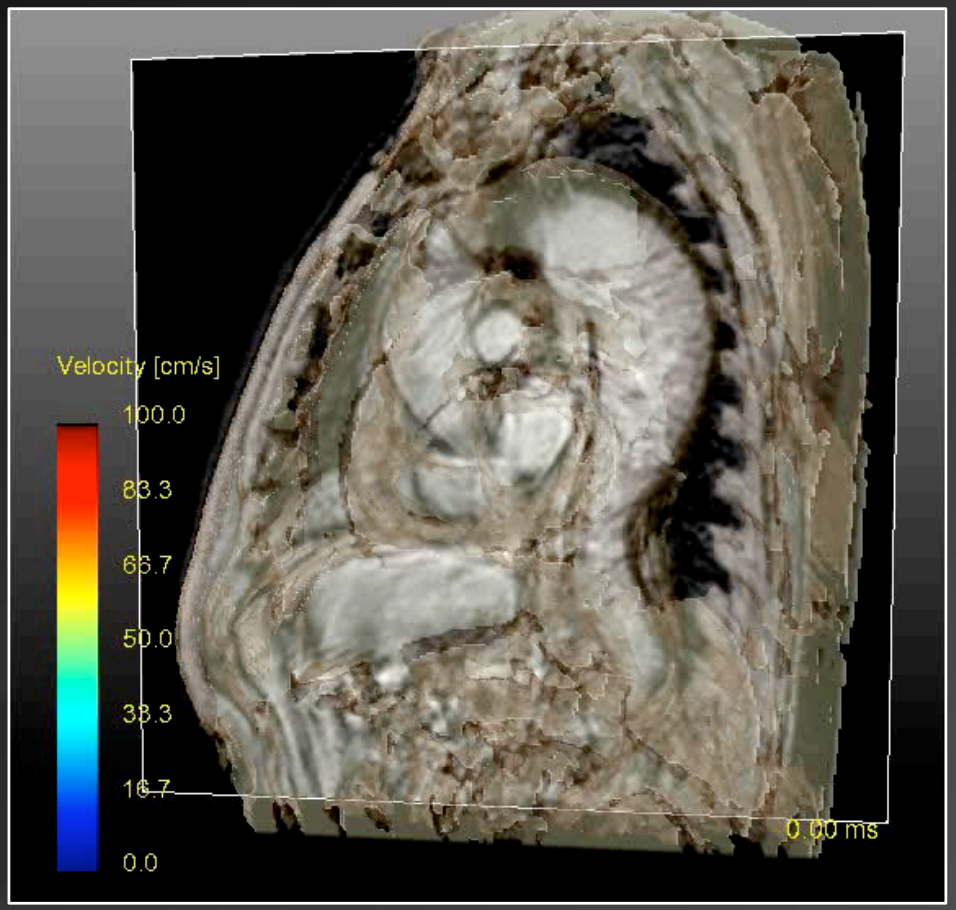
CHUV

Diagnostic Cardiovascular MRI

Function	*Viability*	*Perfusion*
		

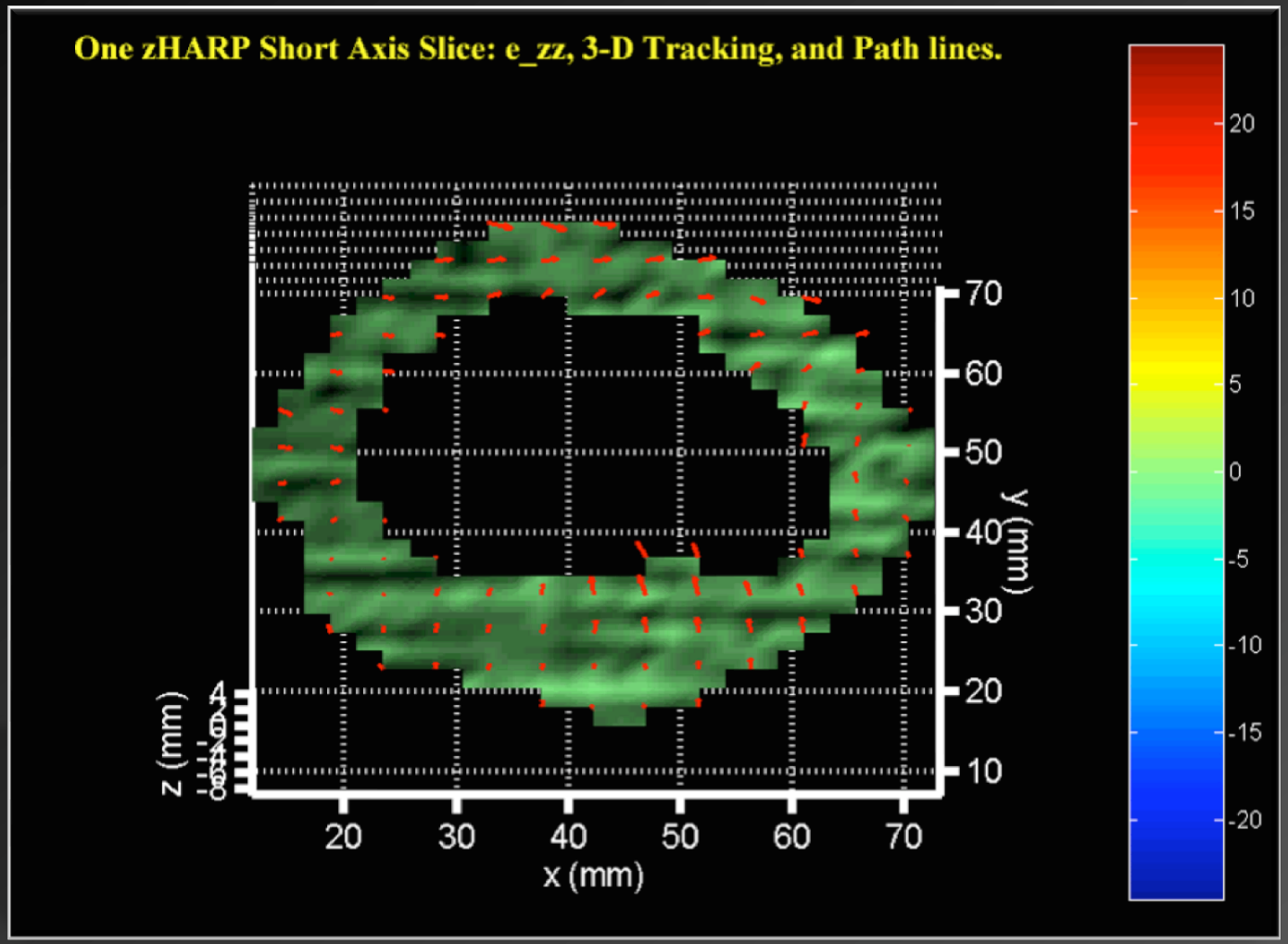
Courtesy: Prof. Jürg Schwitter

Flow Quantification



Courtesy: Dr. Gerard Crelier, Gyrotools, www.gyrotools.com

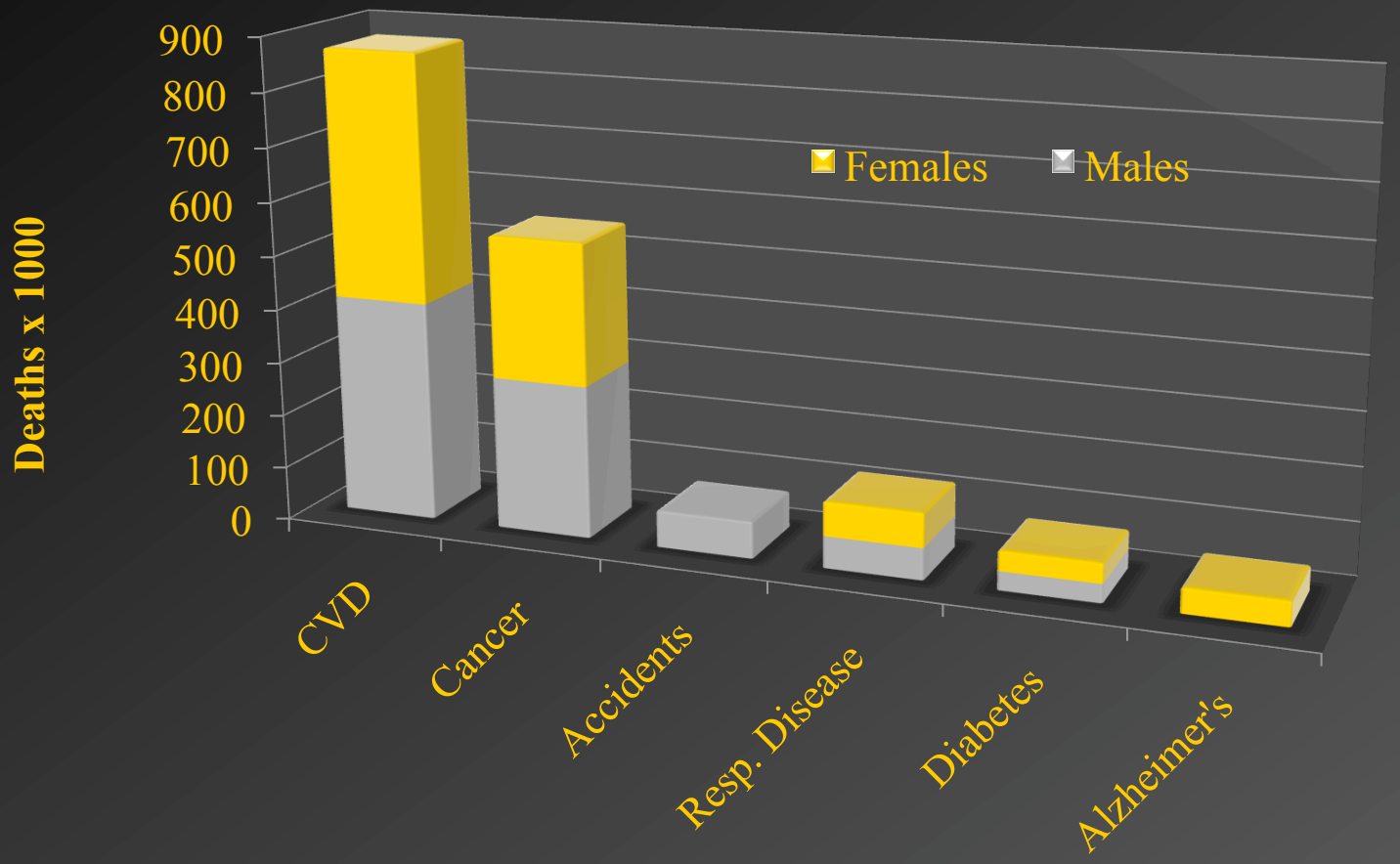
3D Motion of the Heart



Abd-Elmoniem et al.: *Med Image Anal*. 2008 Dec;12(6):778-86.

Human Disease

Leading Causes of Death in the USA in 2004*

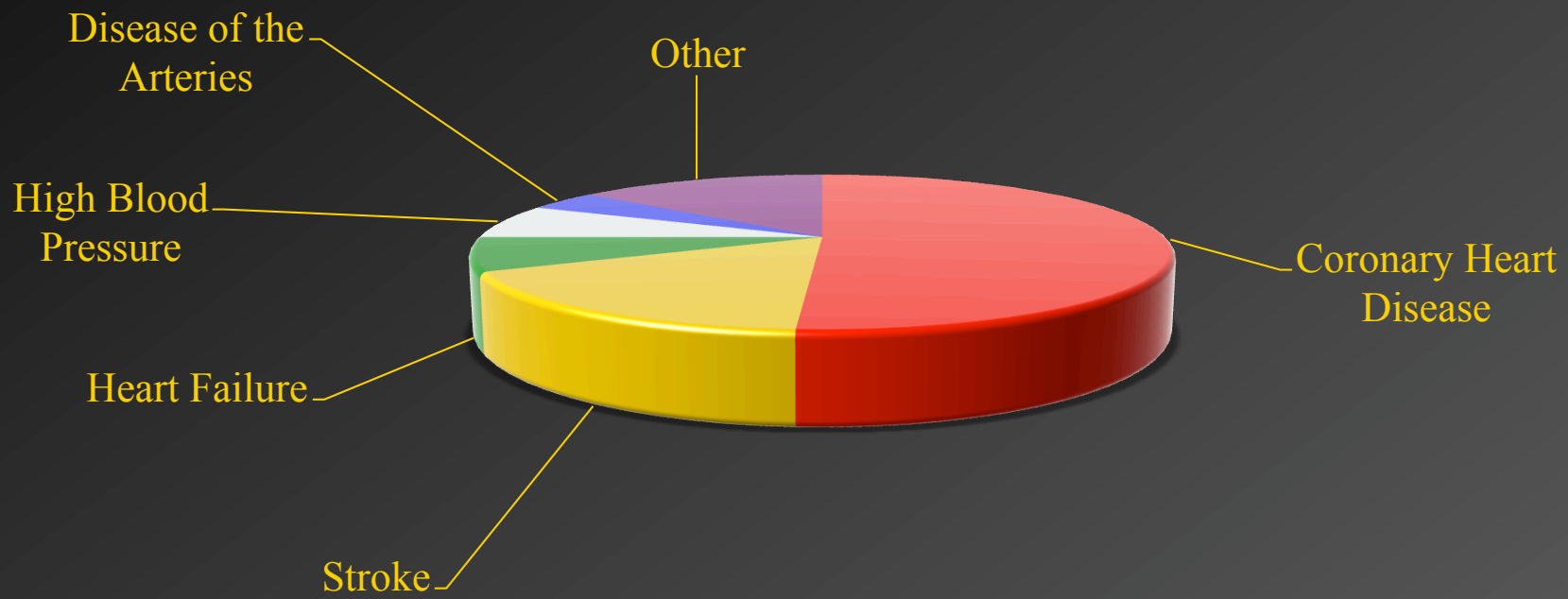


*Heart Disease and Stroke Statistics — 2007 Update, American Heart Association

Cardiovascular Disease

(Leading Cause of Death in Industrialized Nations)

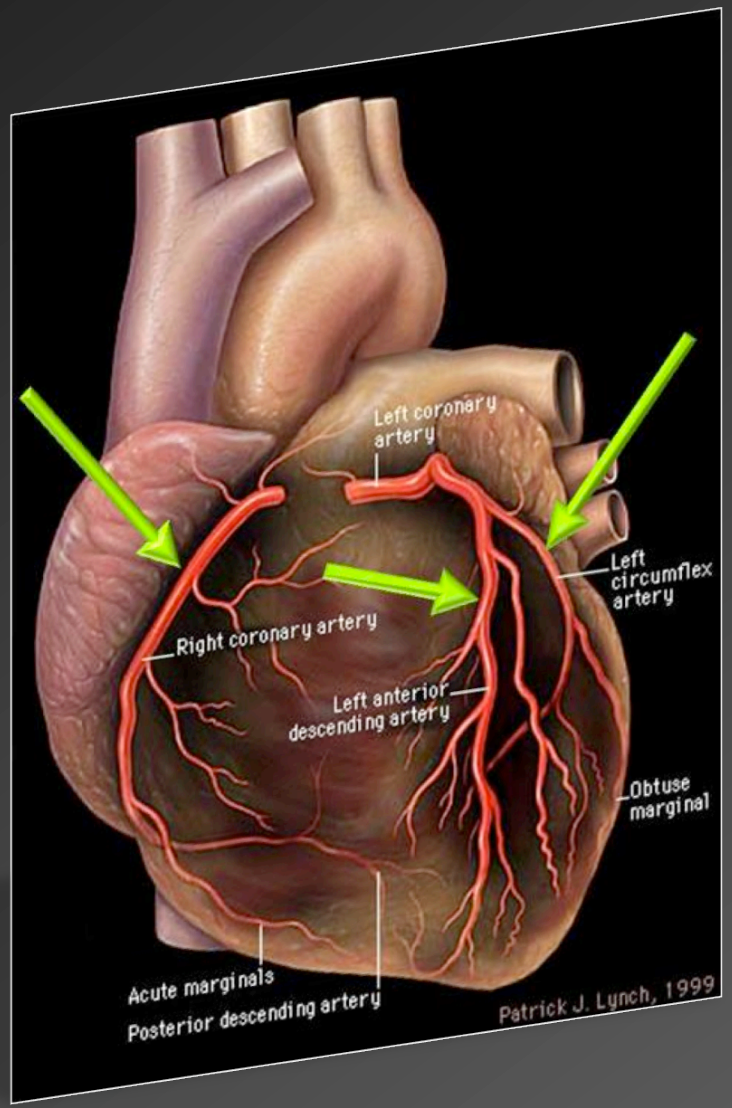
Percentage Breakdown of Deaths (>800’000 in 2006 USA) attributable to CVD*



***Heart Disease and Stroke Statistics — 2010 Update, American Heart Association**

Coronary Arteries

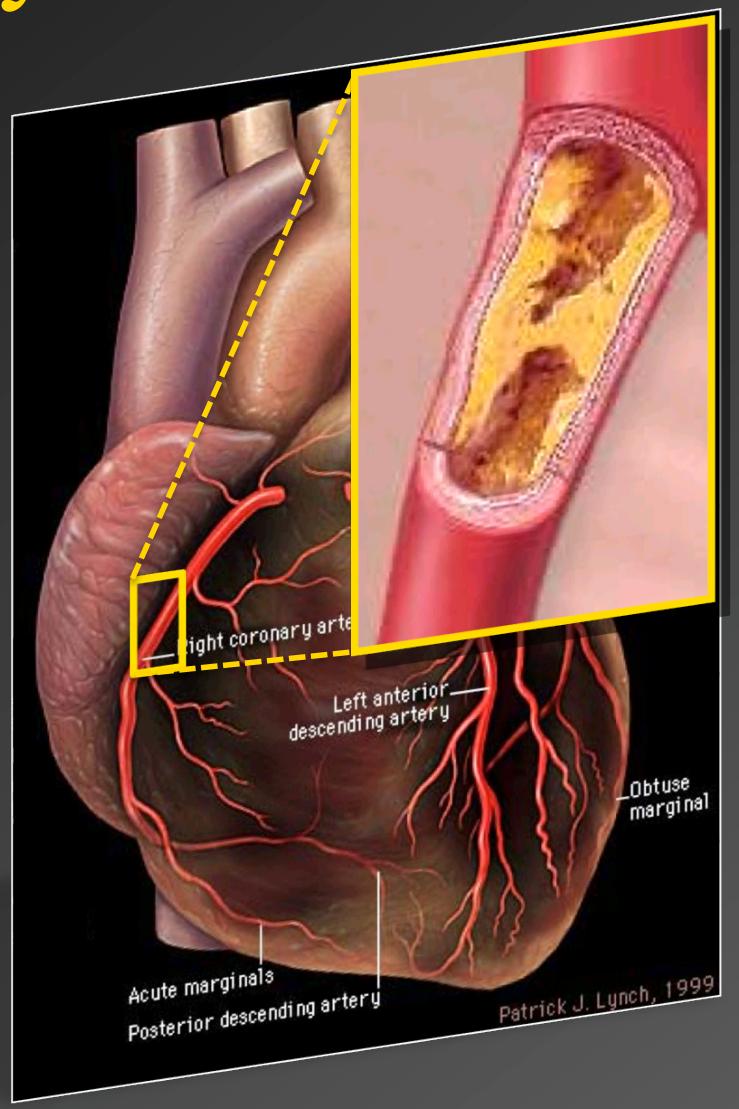
- Blood vessels that supply blood to the heart muscle.



www.info.med.yale.edu

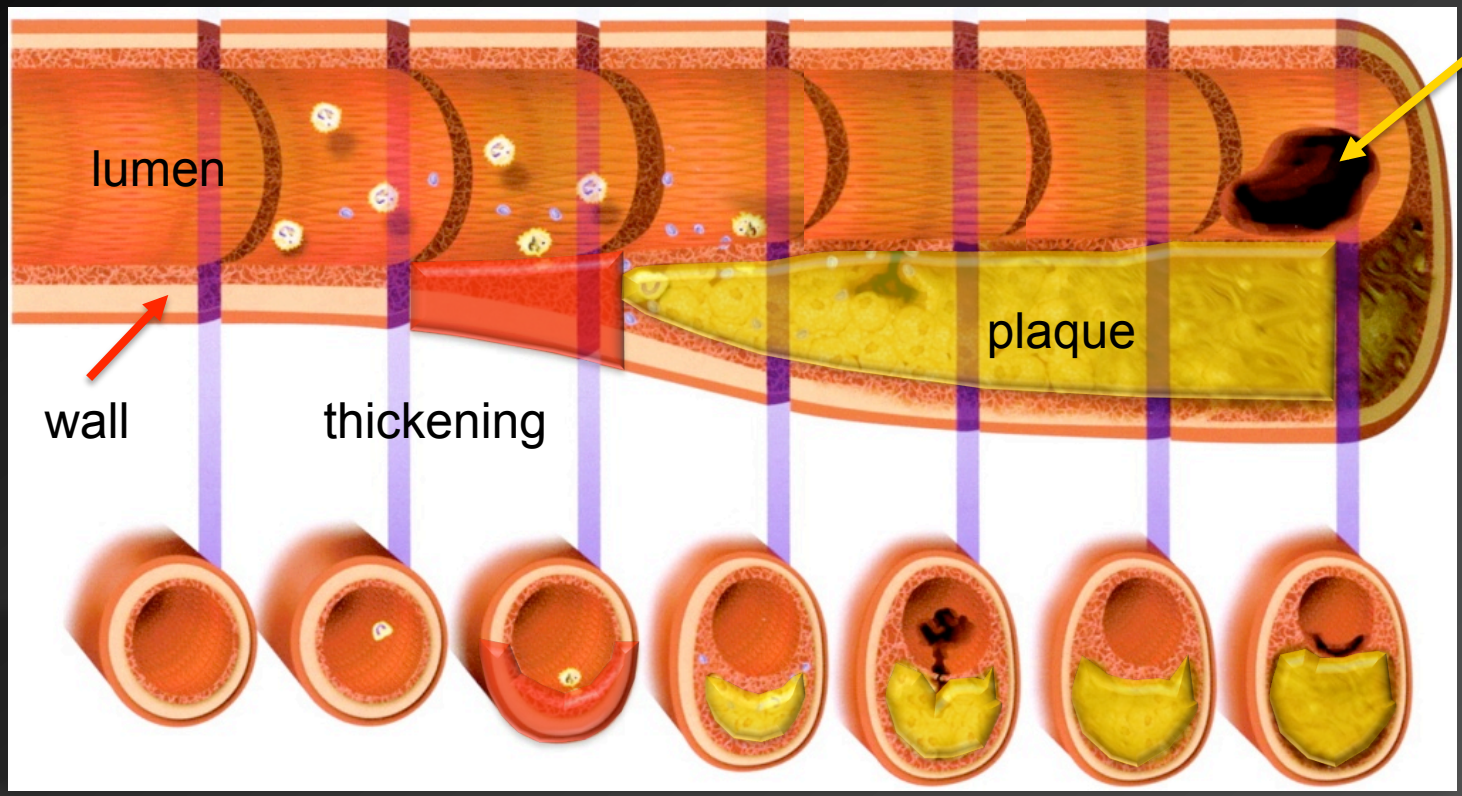
Coronary Artery Disease

- A luminal narrowing (stenosis) develops
- Blood-flow is impaired
- Insufficient oxygen supply
- Angina or infarct



www.info.med.yale.edu

Coronary Artery Disease Progression
(atherosclerosis)

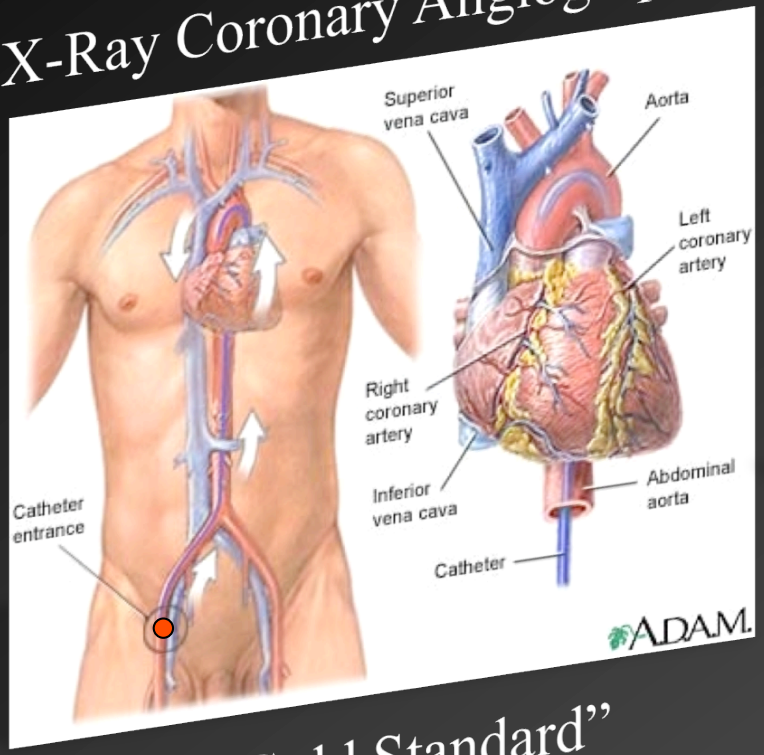


Progression as a function of time

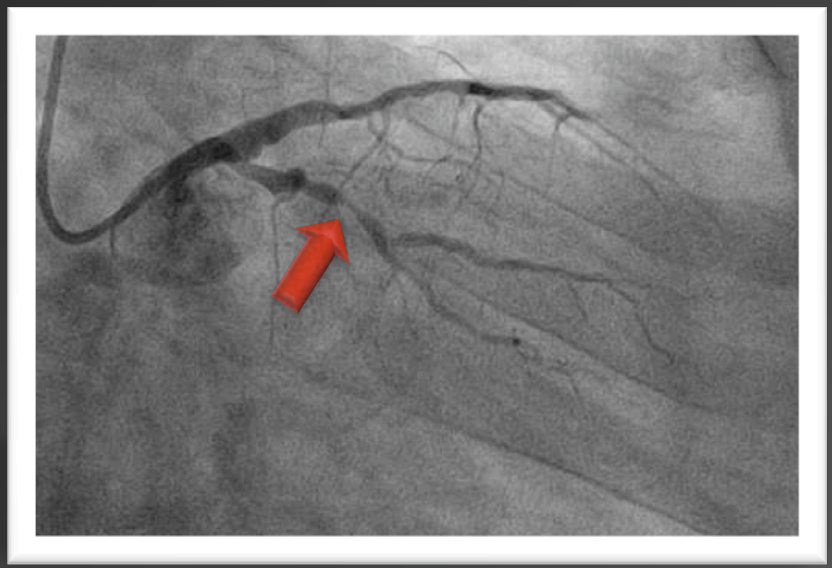
Libby *Circulation* 2001;104:365-72

Diagnosis of Coronary Artery Disease

X-Ray Coronary Angiography



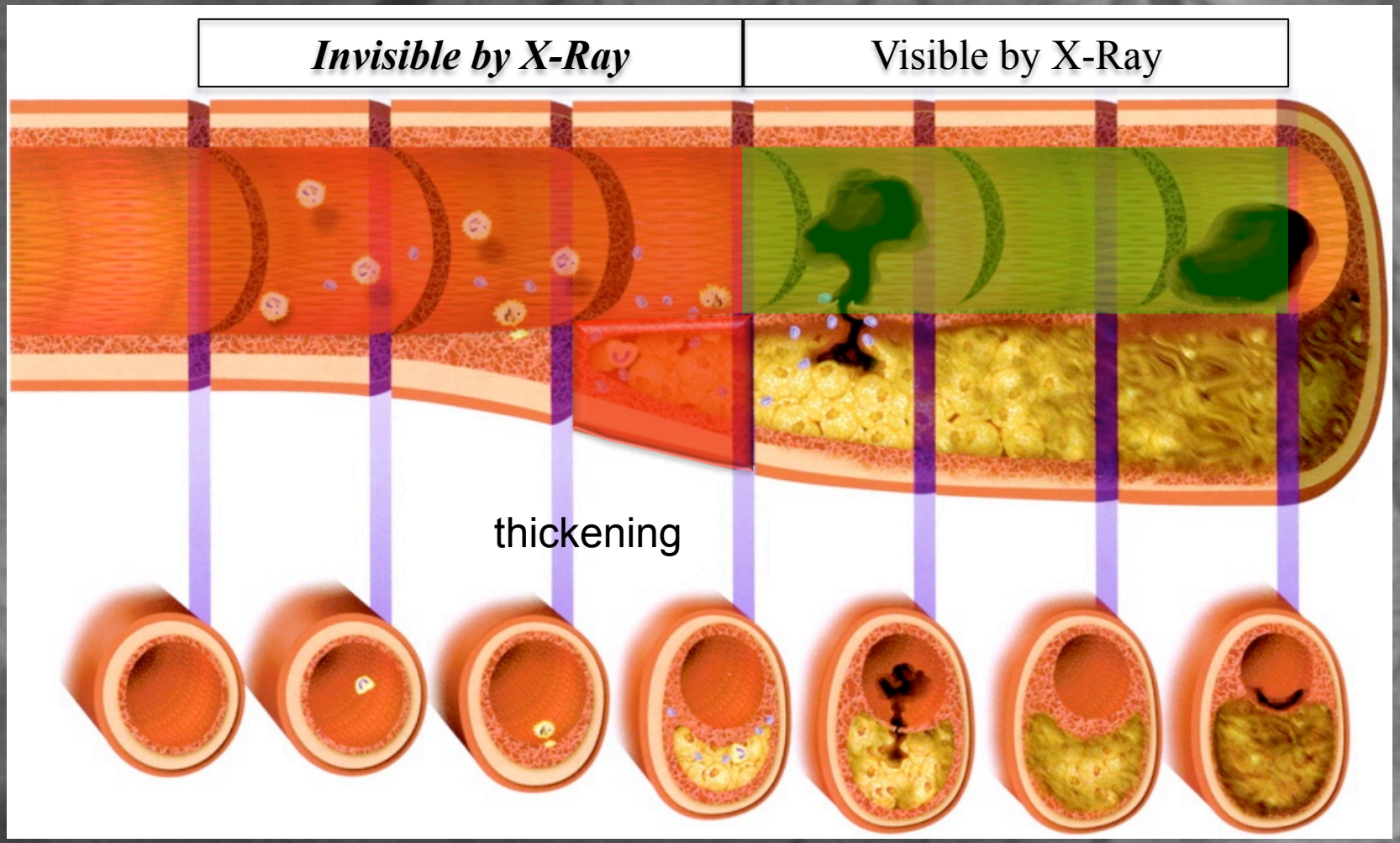
"Gold Standard"



X-Ray
Contrast Agent

Avec l'aimable autorisation de: Dr. Didier Locca

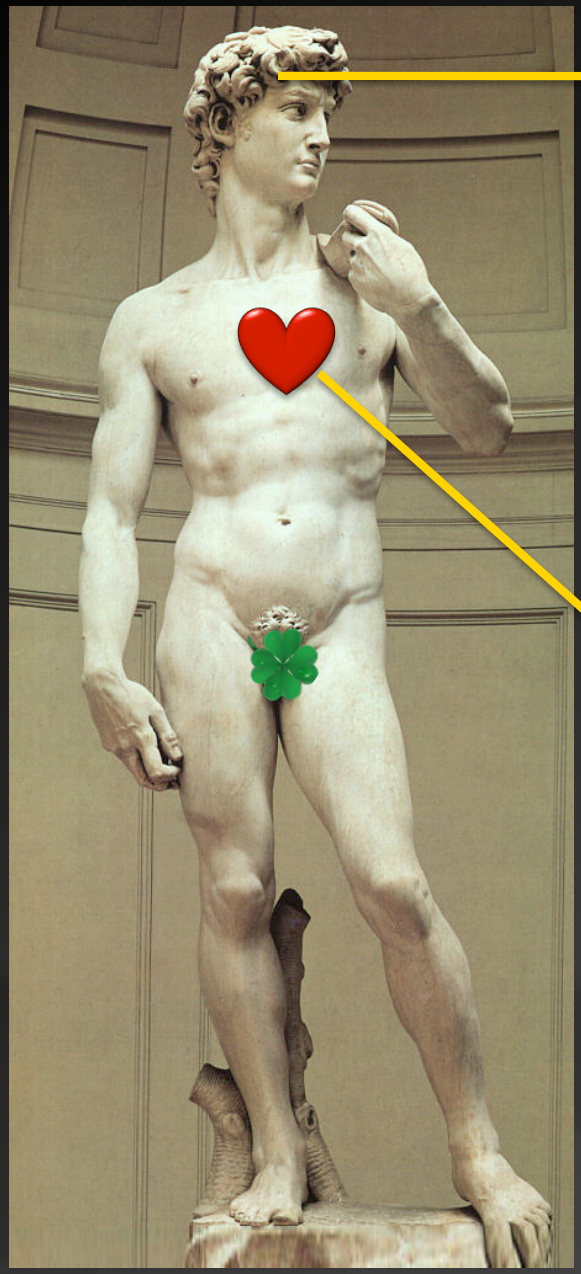
X-Ray Coronary Angiography



*Heart Disease and Stroke Statistics — 2007 Update, American Heart Association

†**Budoff et al. Circulation 1996; 93: 898**

Alternative Comprehensive Technique Needed



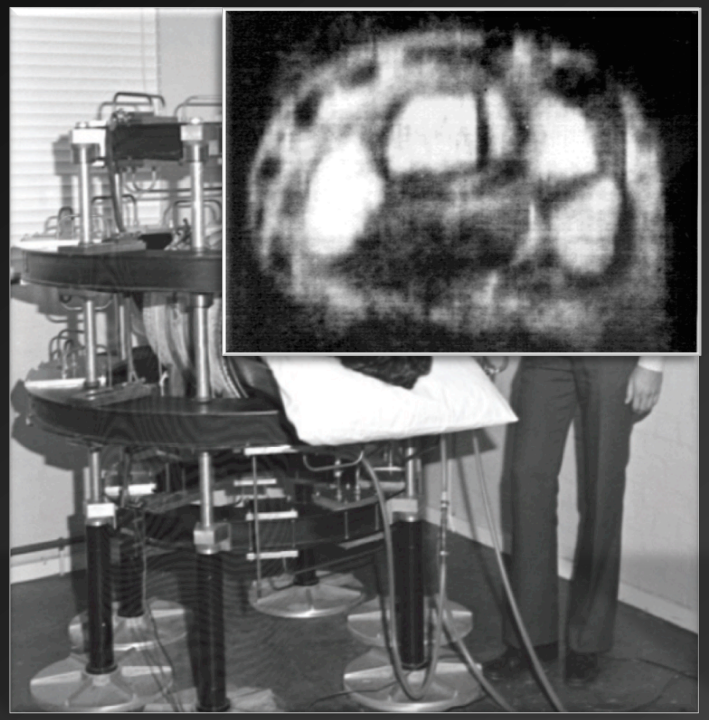
Michelangelo, 1504

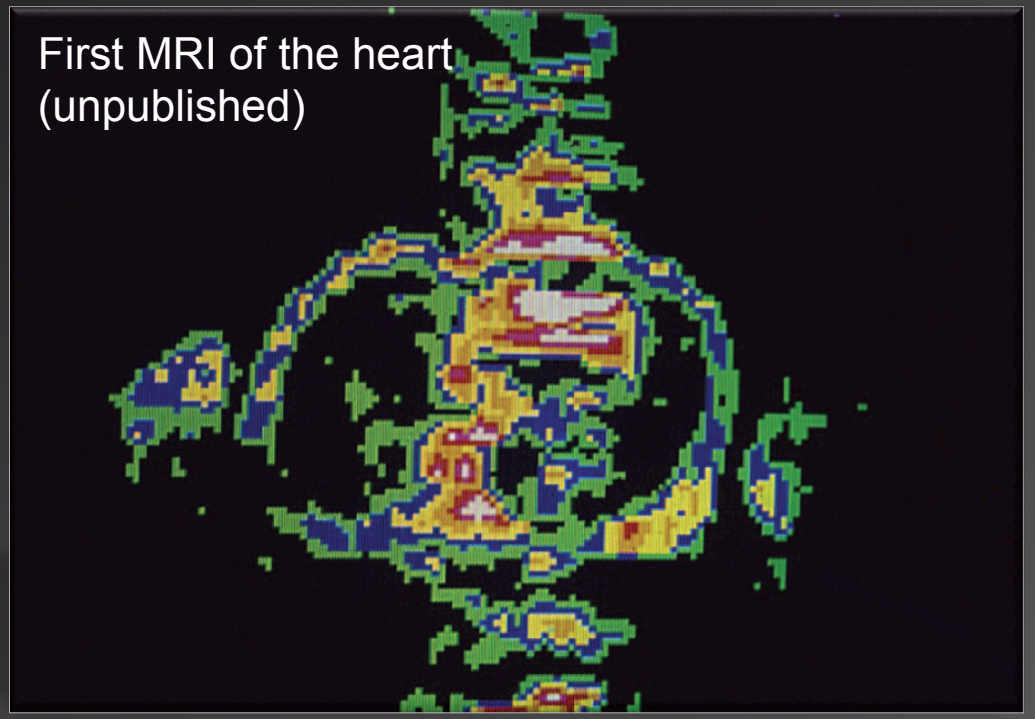
MRI:

- Magnetic field
  - 100’000 x stronger than earth magnetic field.
  - 600 times stronger than fridge magnet.
- No X-Rays
- Non-invasive
- High soft tissue contrast
- Patient friendly

A little Bit of History: 1977

First image of a human heart that I was able to find





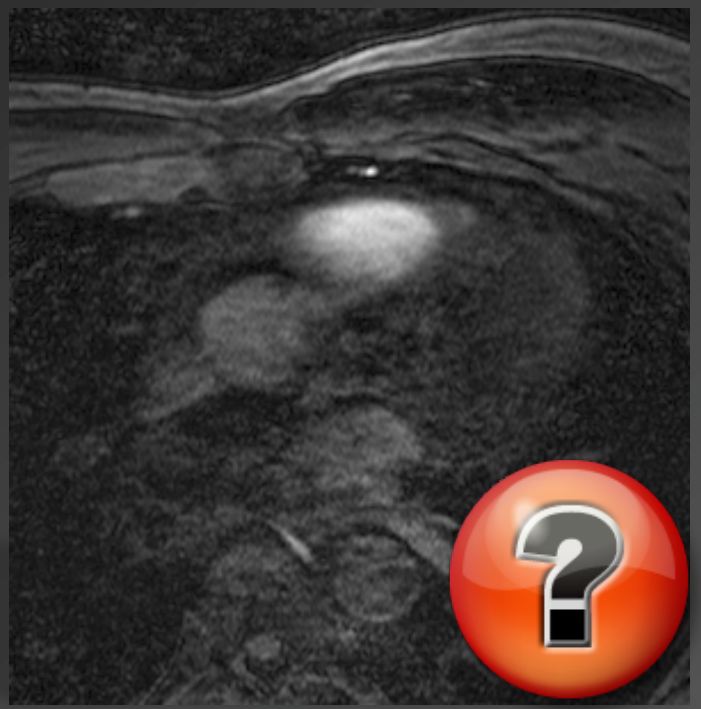
Courtesy: Bill Edelstein & Paul Bottomley

***Hinshaw WS, Bottomley PA et al.: Nature 1977; 270: 722-3**

Magnetic Resonance Imaging (MRI)

Image of a brain

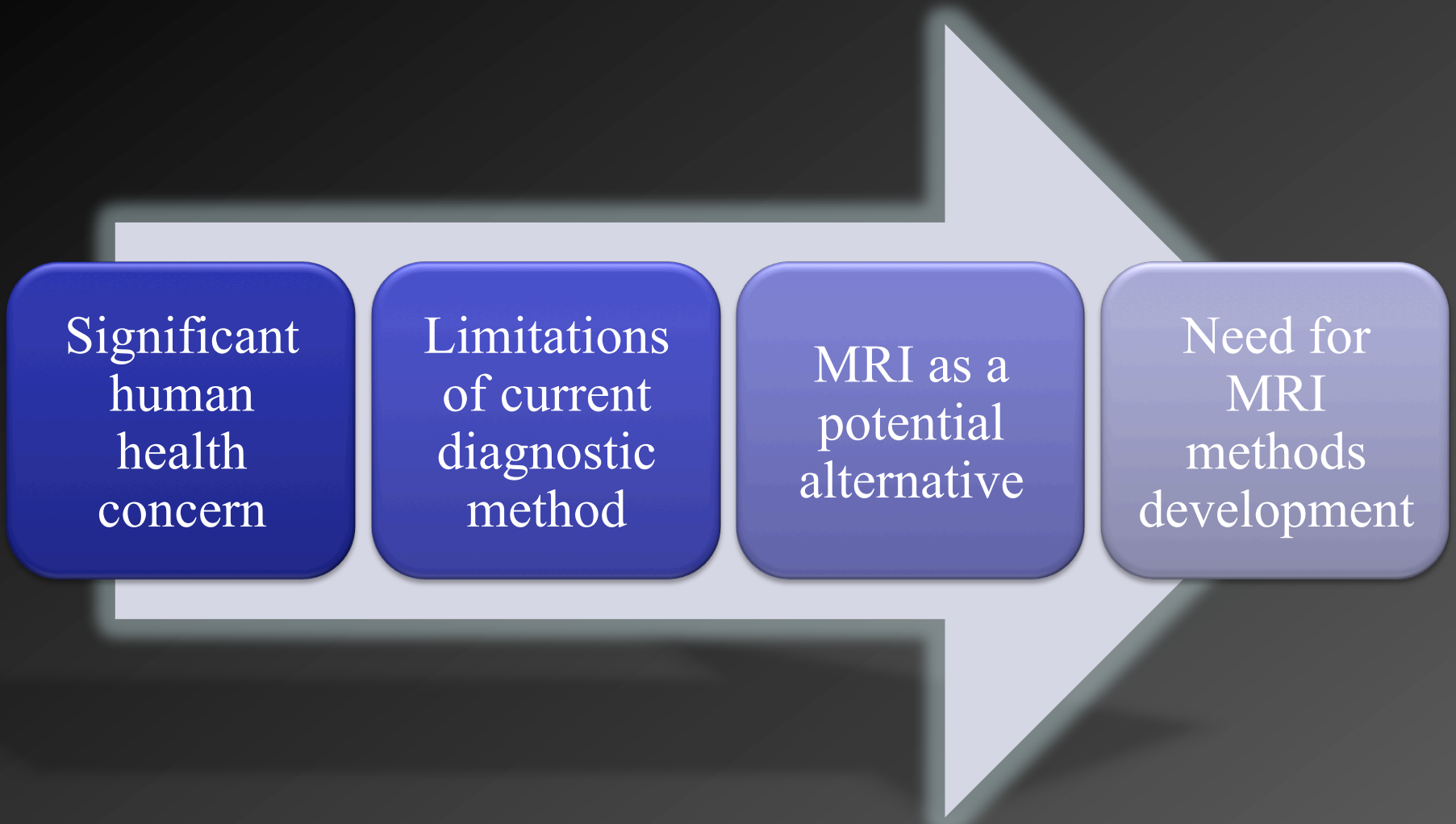
Image of a heart



MRI method:

Optimized to visualize blood-vessels in the brain

We Have Established…



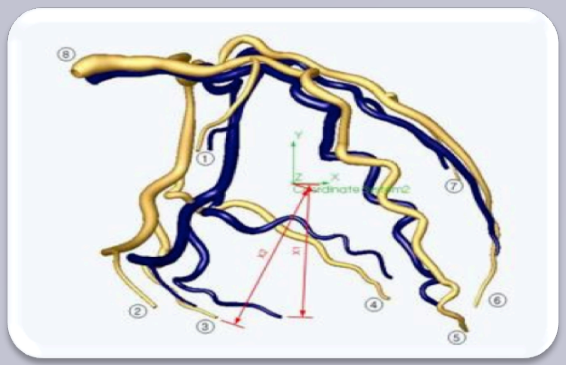
Understand the Problem…

Motion

- Breathing
- Heartbeat

Contrast

- Muscle
- Blood



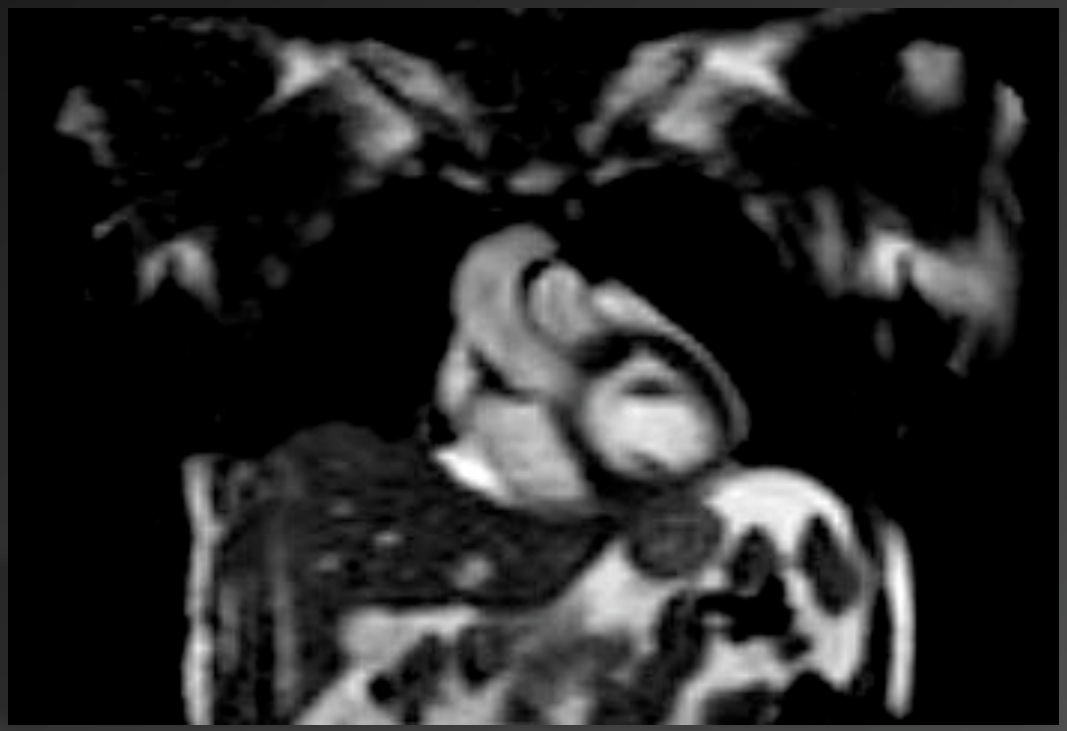
Geometry

- 3D
- Small Ø
- Tortuous

Understanding Motion

Intrinsic ***cardiac motion***: Cardiac cycle: ~60/min; ~2cm
Extrinsic ***cardiac motion***: Respiratory cycle: ~12/min; ~2cm

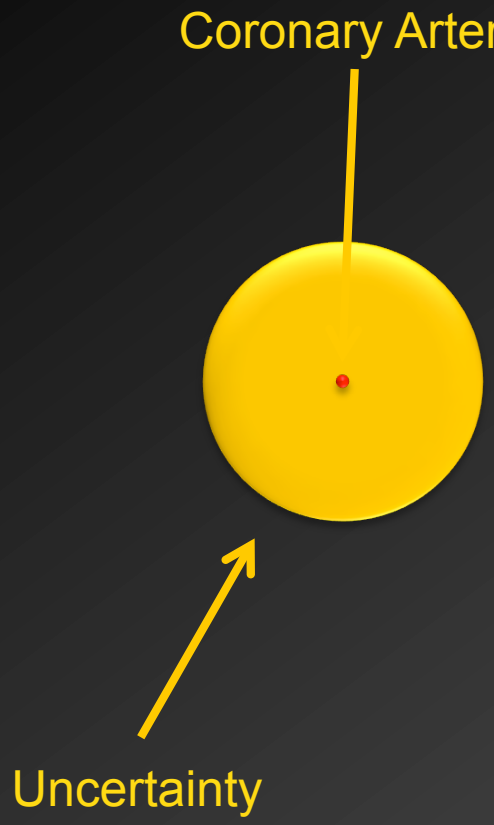
Expiration

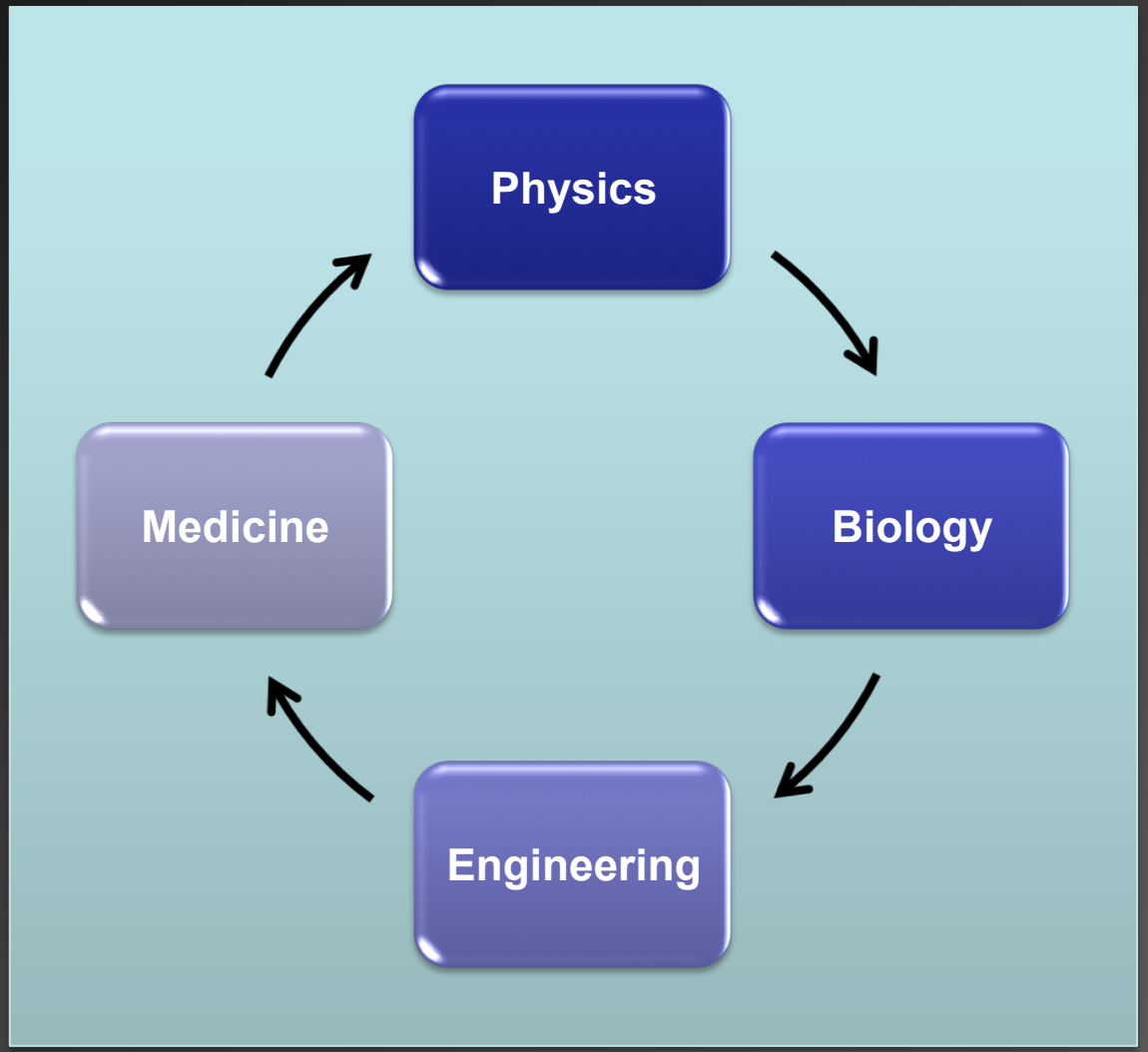


Inspiration

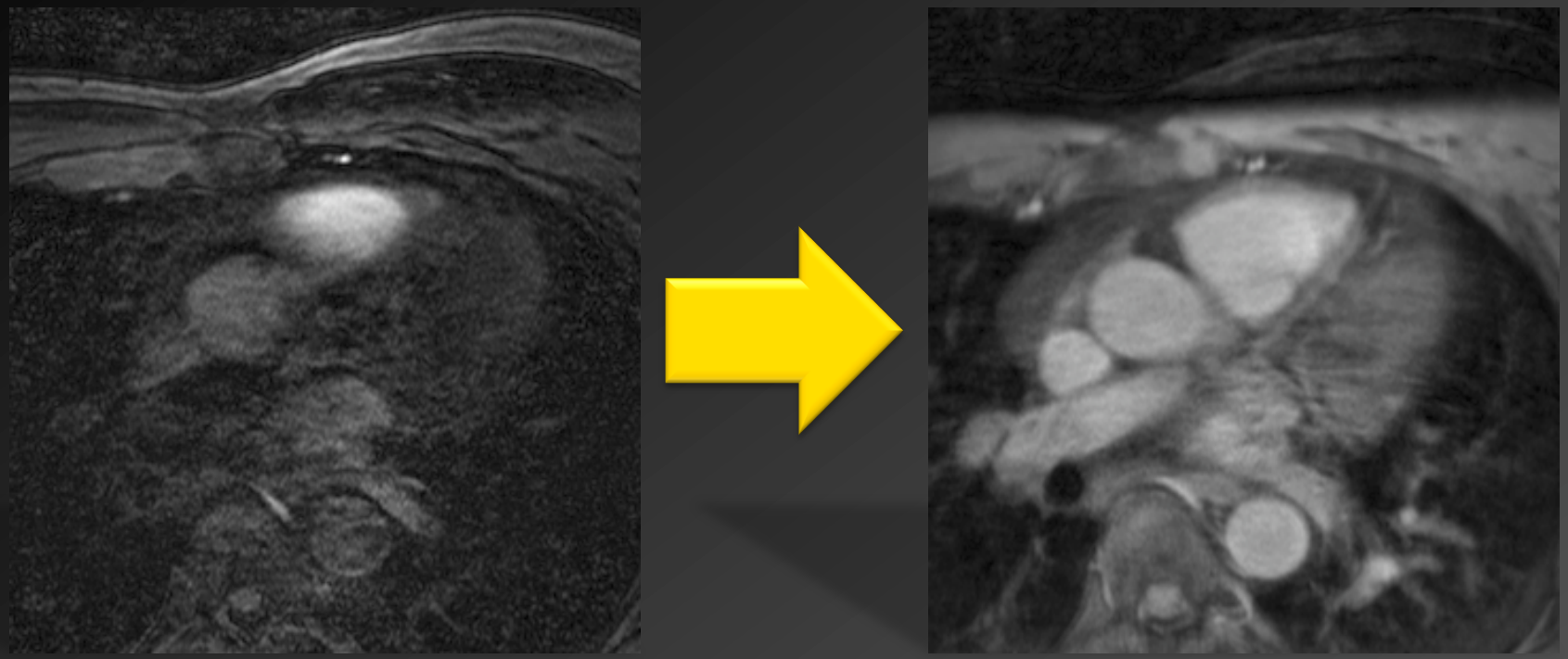
32cm

Engineering Challenge



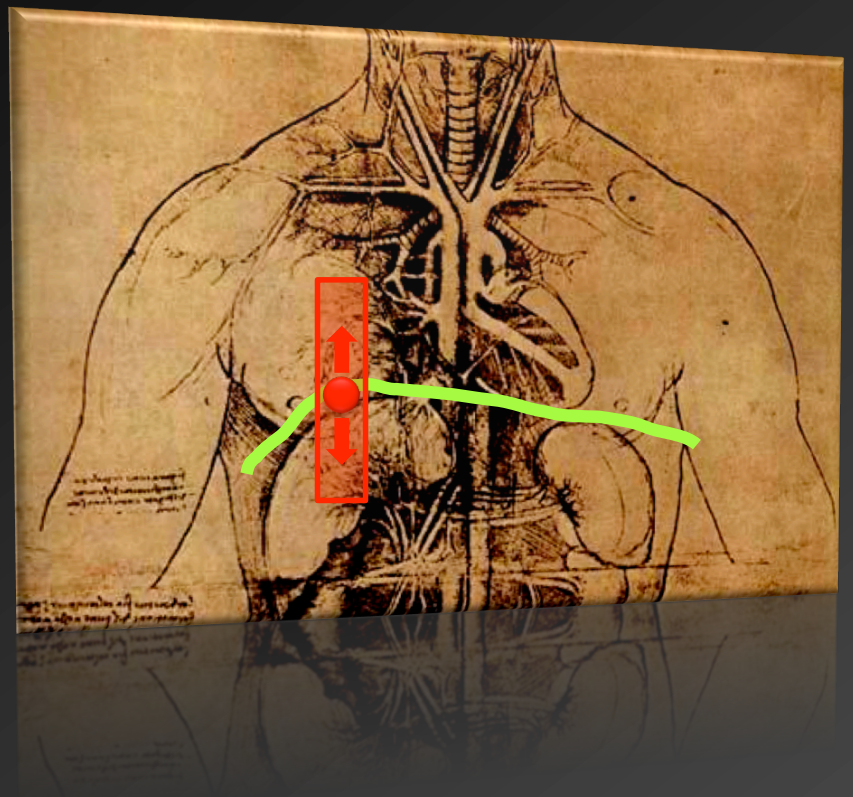


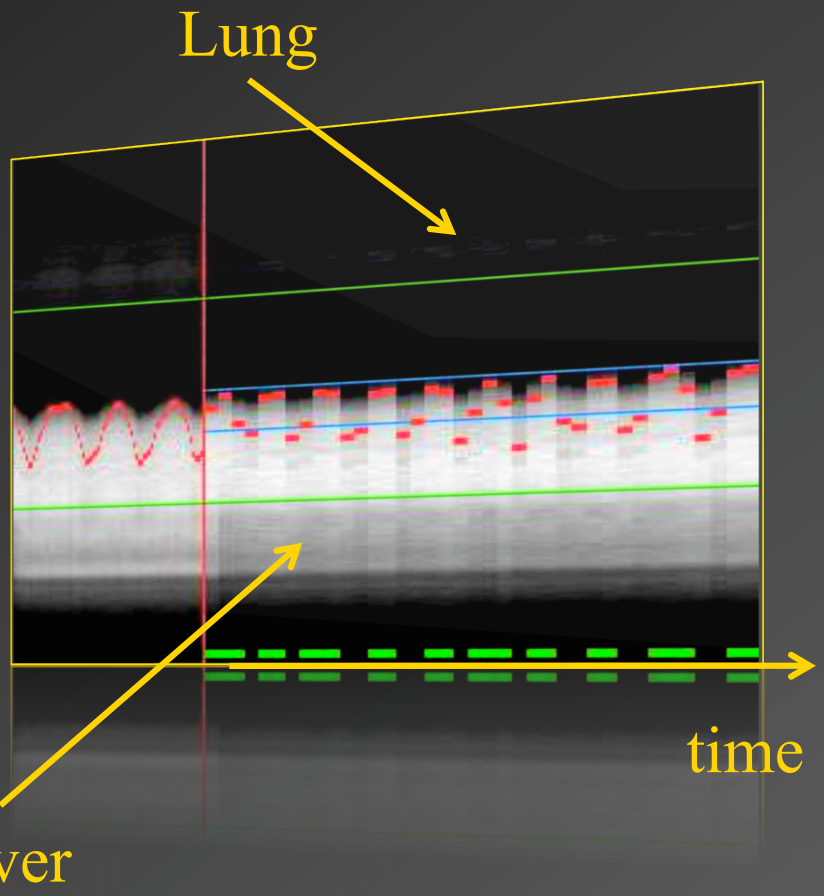
Suppression of Motion (Intrinsic)



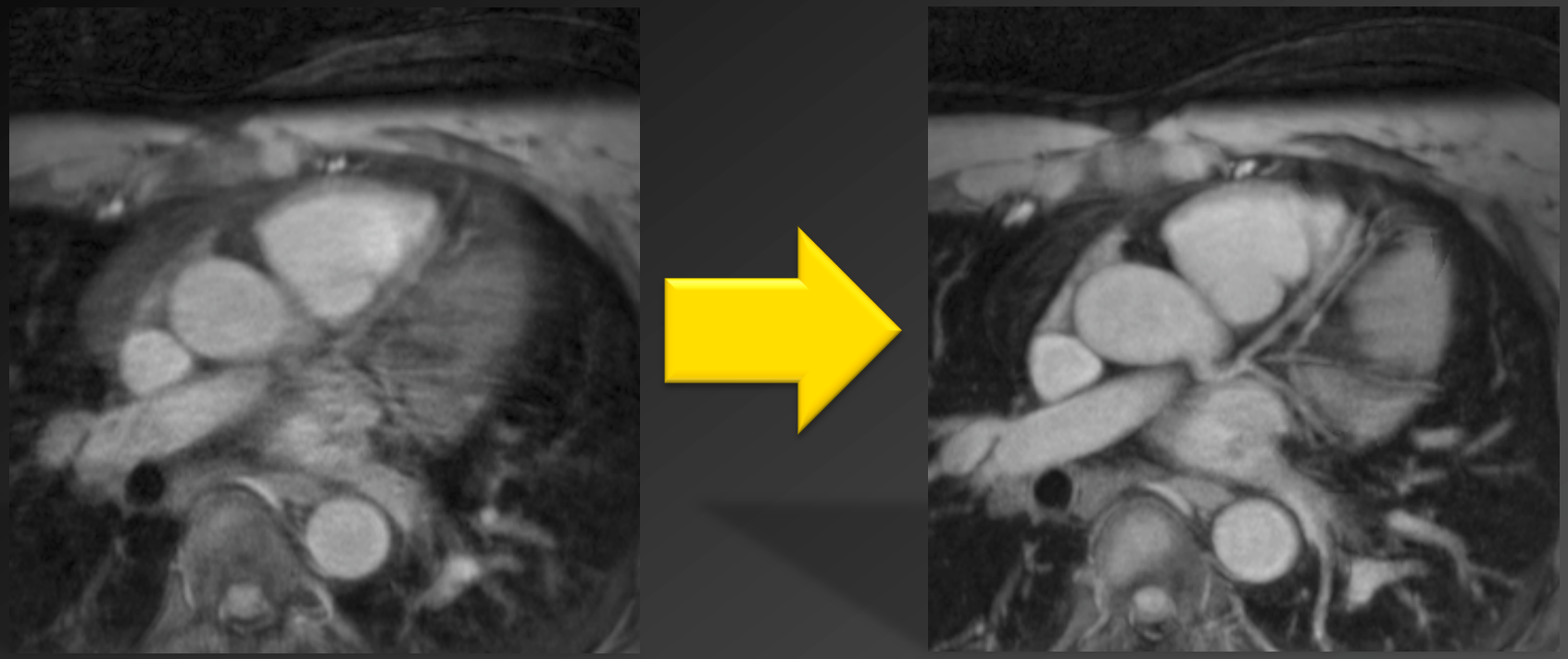
- ECG triggering and segmented acquisition
- Short data collection window
- Data collection during a period of minimal motion

Suppression of Motion (Extrinsic)



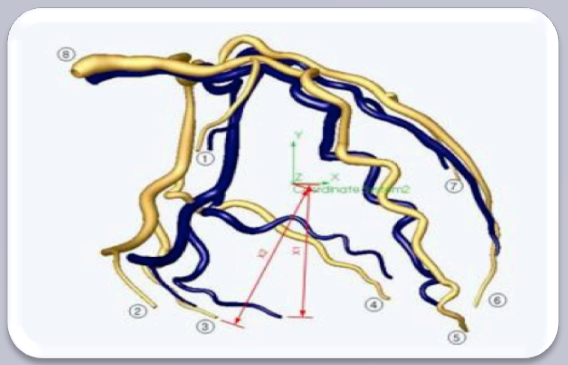


Suppression of Motion (Extrinsic)



- Navigator gating during free-breathing

Understand the Problem…



Motion

- Heartbeat
- Breathing

Contrast

- Muscle
- Blood

Geometry

- 3D
- Small Ø
- Tortuous

Generation of Contrast

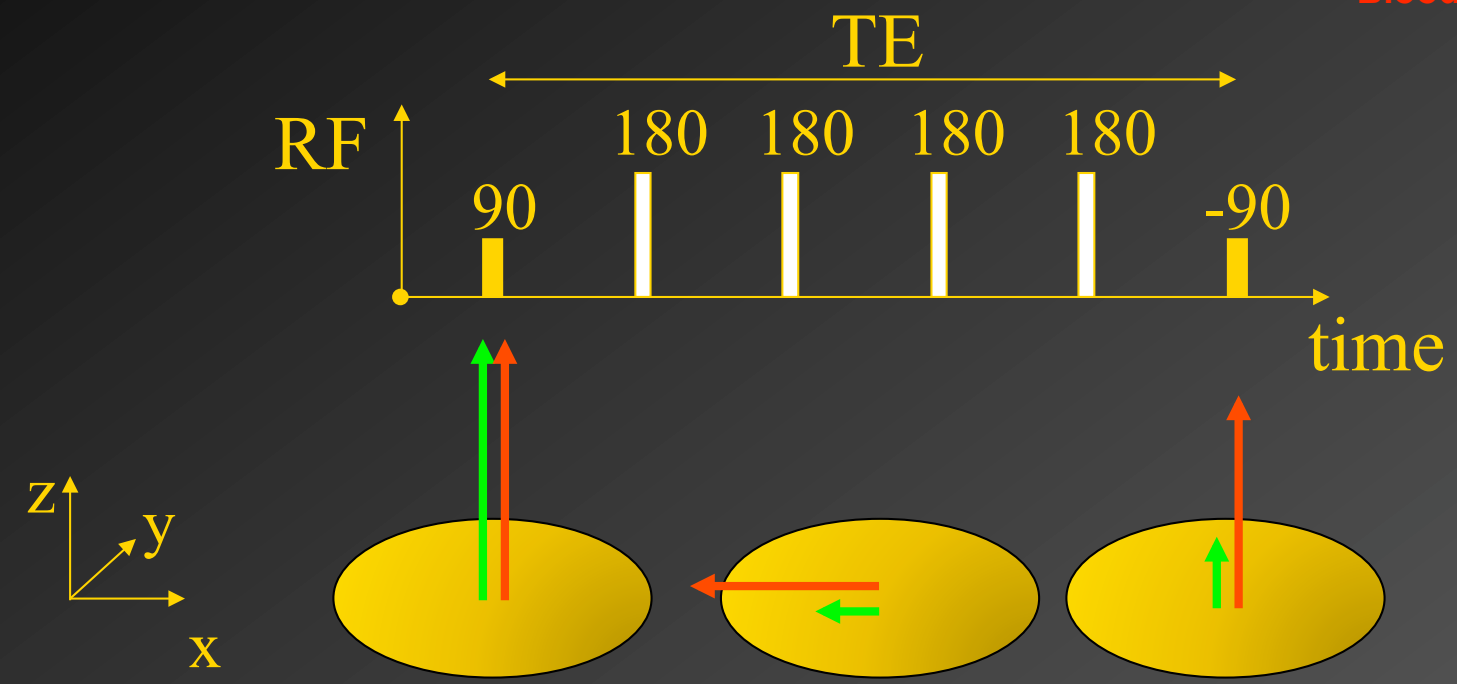
	T1 [ms]	T2 [ms]	$\Delta\omega_0$ [Hz]	flow
Blood	1650	250	0	yes
Muscle	1200	50	0	no
Fat	300	100	440	no

Generation of Contrast

- T2 Prep*

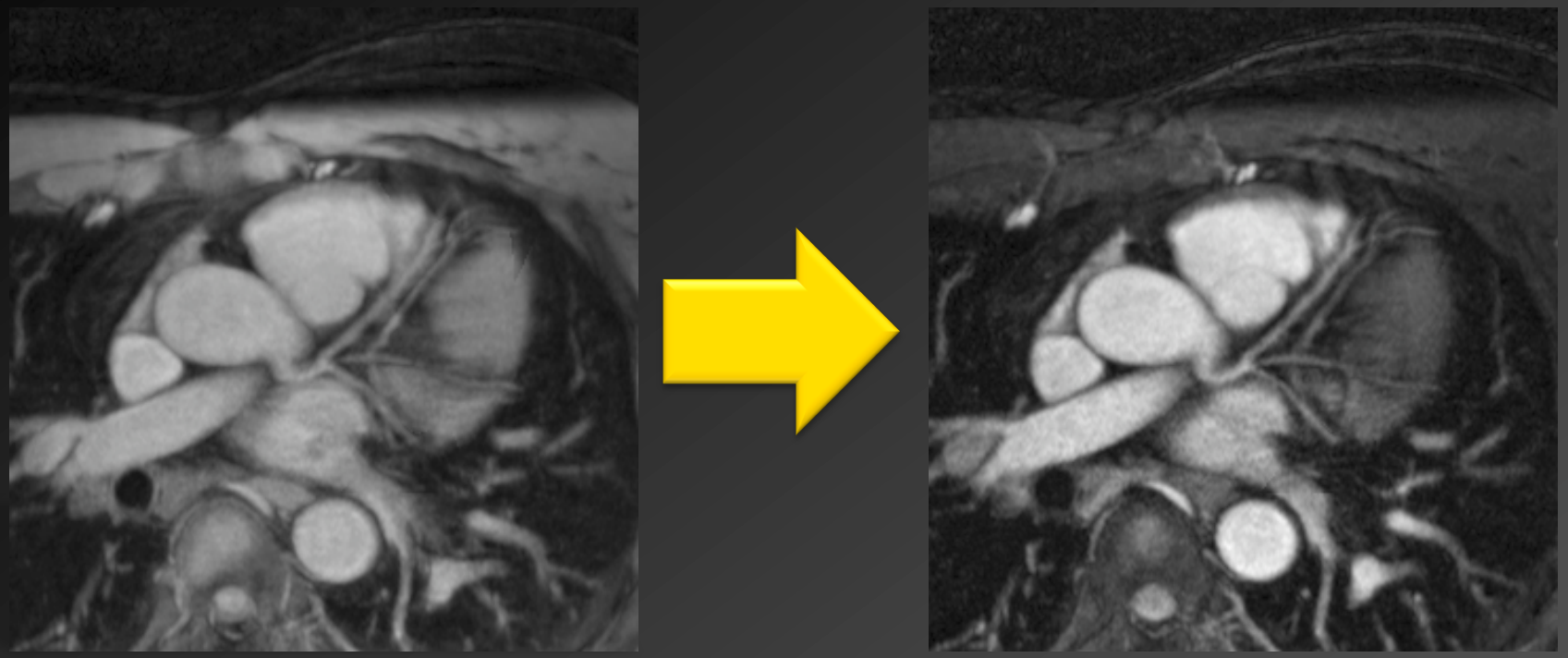
$T2_{Myo}$: 50ms

$T2_{Blood}$: 250ms



*GA Wright, DG Nishimura, A Macovski, *Magn Reson Med* 17:126-140 (1991).
*JH Brittain, et al., *Magn Reson Med* 33:689-696 (1995).

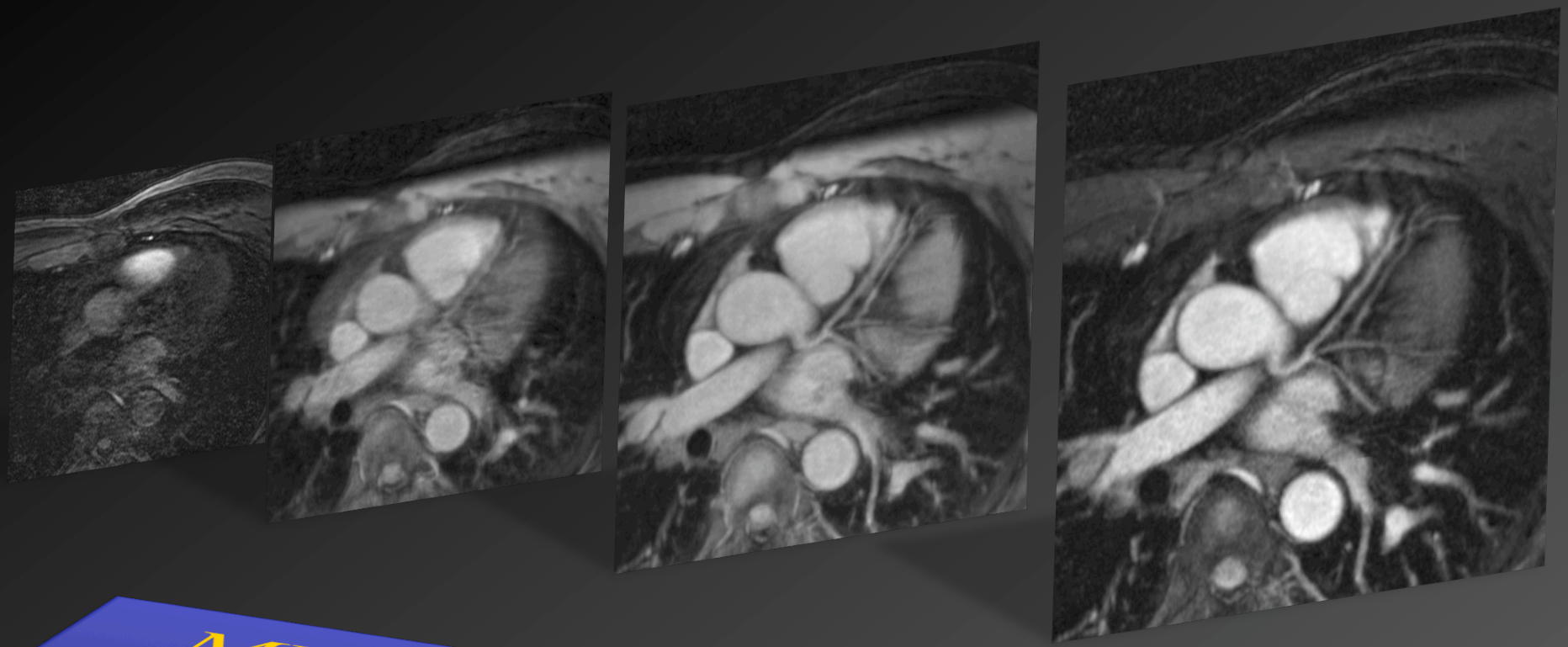
Generation of Contrast



- Taking Advantage of Natural T2 differences: T2Prep*

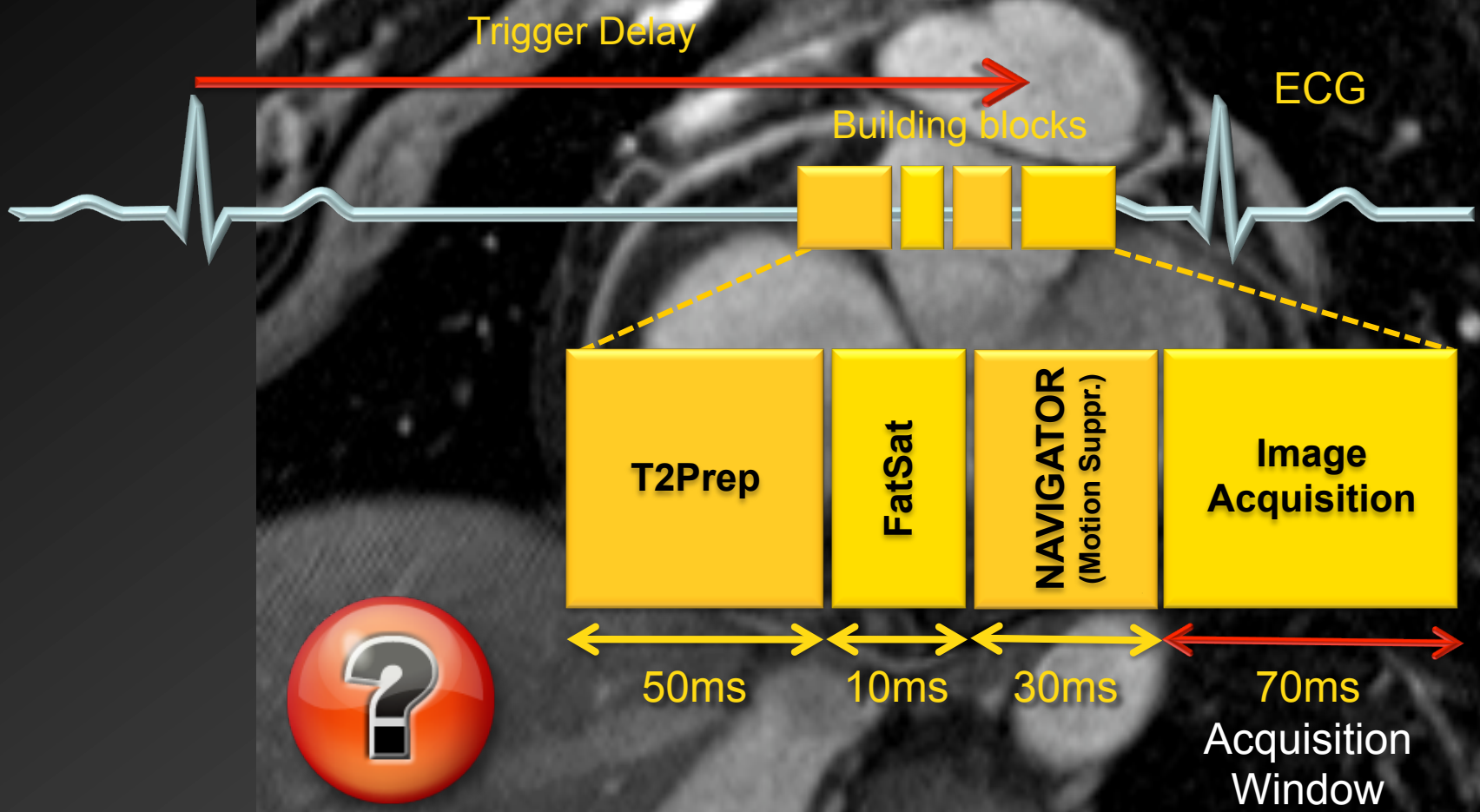
*GA Wright, DG Nishimura, A Macovski, *Magn Reson Med* 17:126-140 (1991).
*JH Brittain, et al., *Magn Reson Med* 33:689-696 (1995).

Solving the Problem



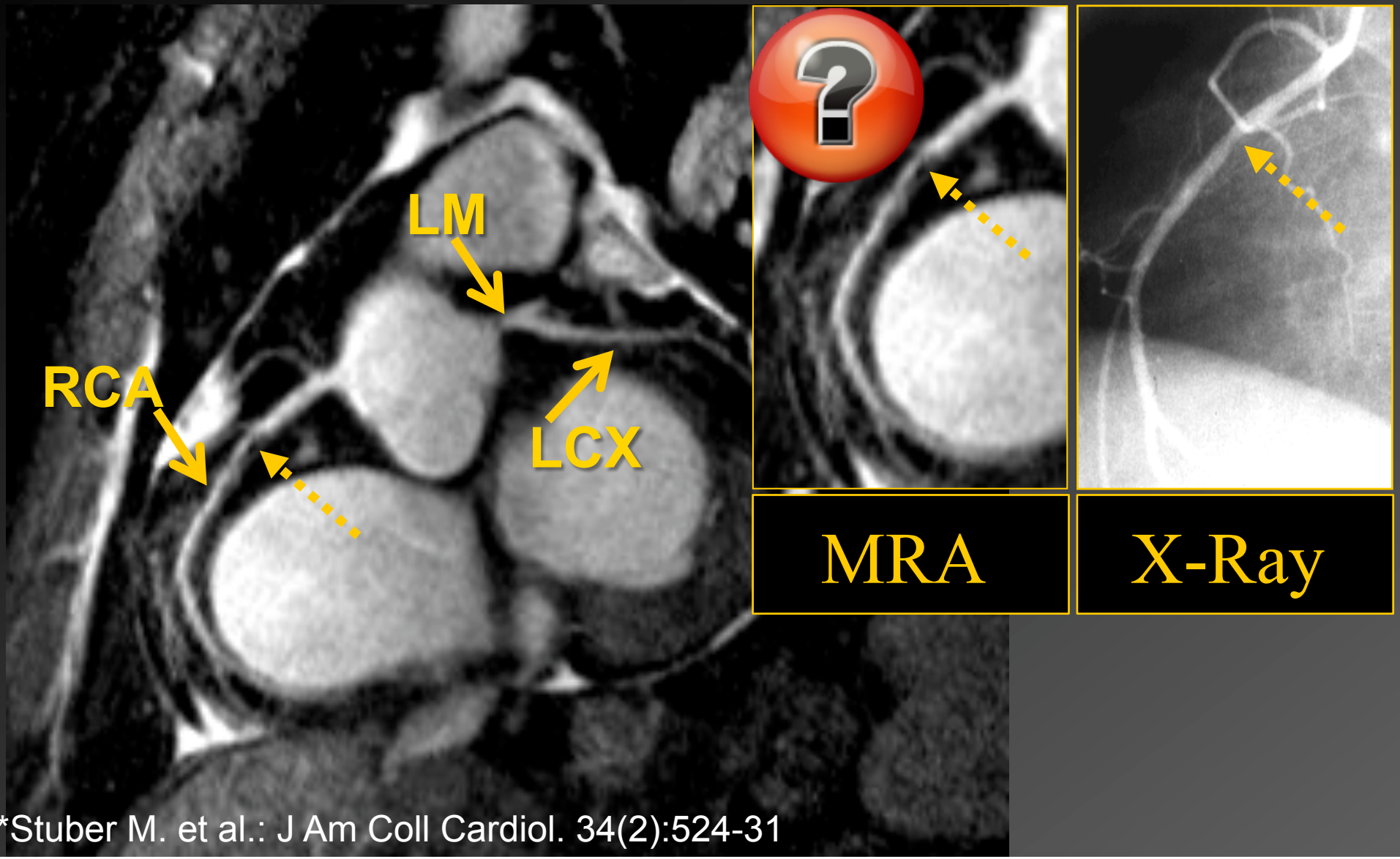
MRI Methods Development

Pulse Sequence for Coronary MRI



1) Stuber M, Botnar RM, Danias PG et al.: *J Am Coll Cardiol*; 34(2):524-531 (1999).

Can the Method Visualize Disease?



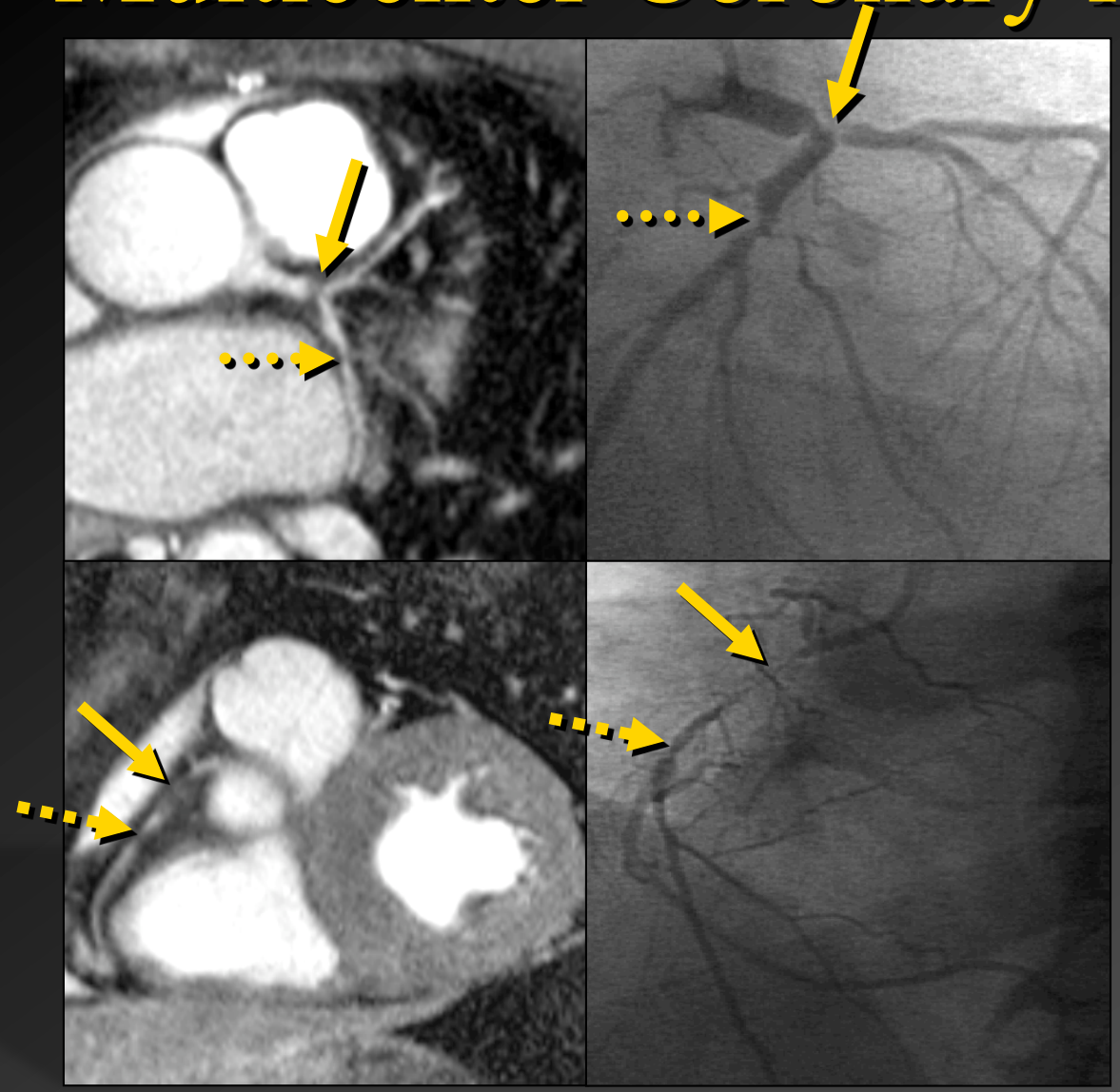
*Stuber M. et al.: J Am Coll Cardiol. 34(2):524-31

Multicenter Coronary MRA Study

- Disseminate MRI method* among international centers
- Purpose & study protocol
  - Using uniform hardware, software & MRI method to examine the clinical value of coronary MRA for the diagnosis of significant disease of the proximal coronary arteries.
  - Prospective comparison with gold standard X-Ray coronary angiography (independent core lab).
  - 109 patients from 8 international centers.

*Stuber M. et al.: J Am Coll Cardiol. 1999 Aug;34(2):524-31

Multicenter Coronary MRA Study



Patient with LM/LAD & LCX disease

Patient with 2 lesions in proximal RCA

1) Kim WY, Danias PG, Stuber M. et al.: *N Engl J Med*;345(26):1863-1869 (2001).

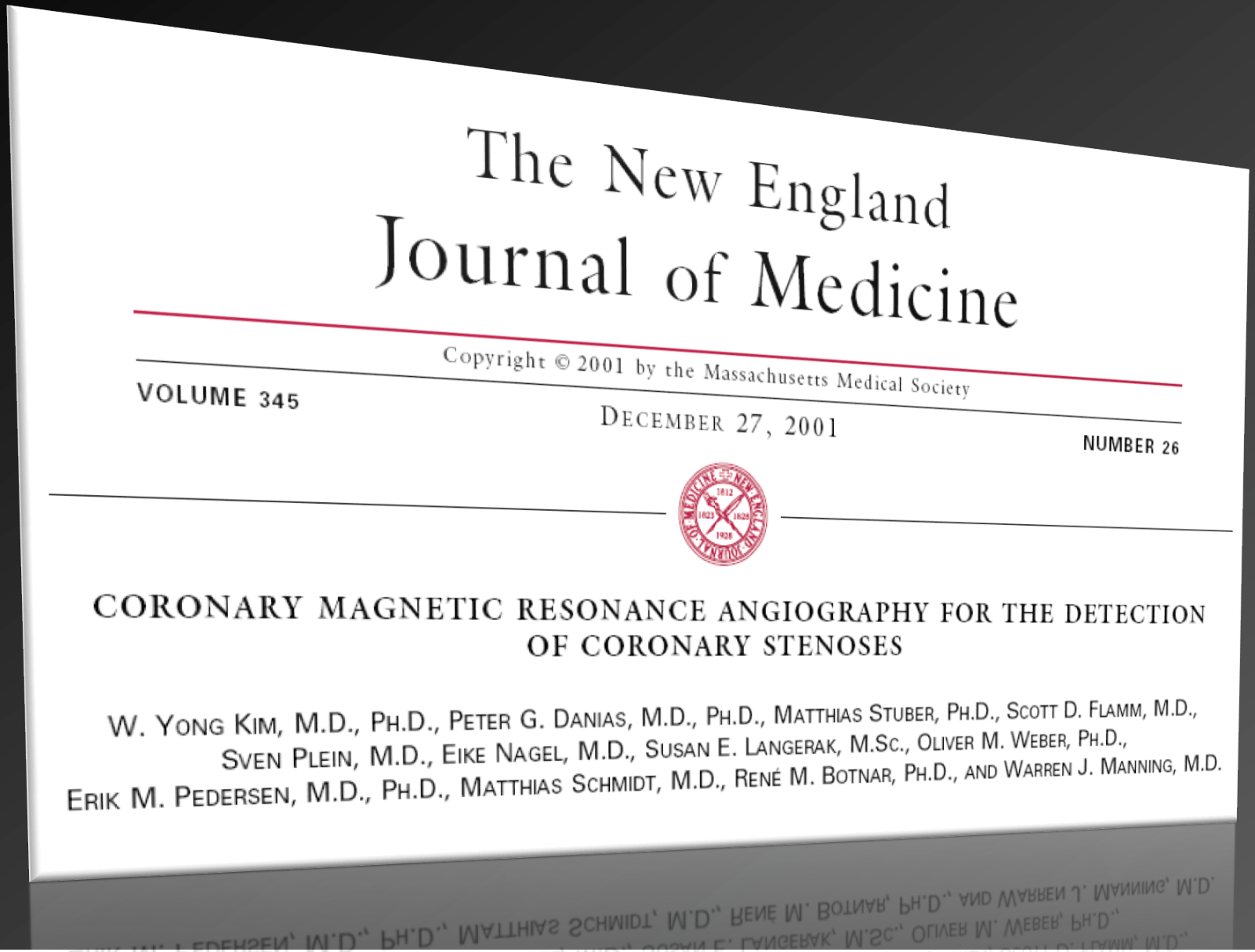
Multicenter Coronary MRA Study

- Results (Detection of >50% stenosis)

	Any CAD [%]	LM/3VD [%]
Sensitivity	93	100
Specificity	42	85
PPV	70	54
NPV	81	100

1) Kim WY, Danias PG, Stuber M. et al.: *N Engl J Med*;345(26):1863-1869 (2001).

Multicenter Coronary MRA Study



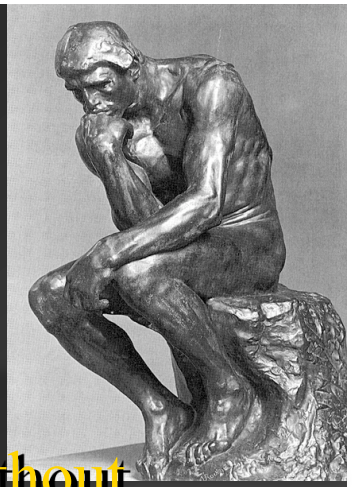
The New England Journal of Medicine

VOLUME 345 DECEMBER 27, 2001 NUMBER 26

CORONARY MAGNETIC RESONANCE ANGIOGRAPHY FOR THE DETECTION OF CORONARY STENOSES

W. YONG KIM, M.D., PH.D., PETER G. DANIAS, M.D., PH.D., MATTHIAS STUBER, PH.D., SCOTT D. FLAMM, M.D., SVEN PLEIN, M.D., EIKE NAGEL, M.D., SUSAN E. LANGERAK, M.SC., OLIVER M. WEBER, PH.D., ERIK M. PEDERSEN, M.D., PH.D., MATTHIAS SCHMIDT, M.D., RENÉ M. BOTNAR, PH.D., AND WARREN J. MANNING, M.D.

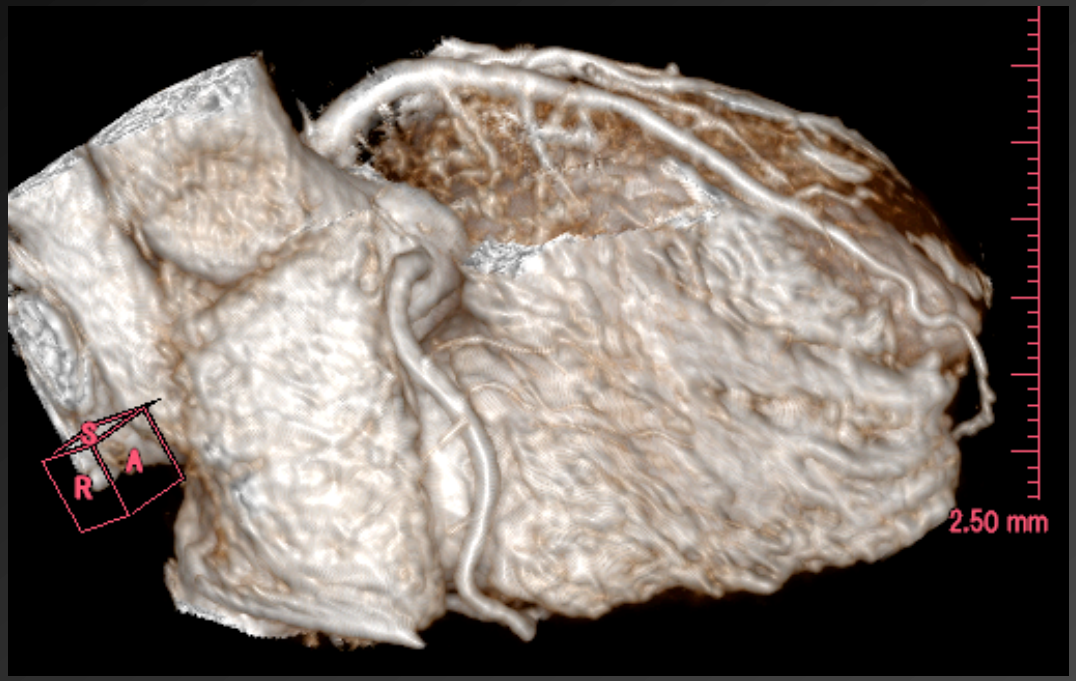
Time to Reflect…



- What have we learned?
  - MRI, a non-invasive, patient-friendly technique without x-ray exposure, enables the assessment of significant proximal *luminal* coronary artery disease.
- What is needed to take this to the next level?
  - Obtain a higher specificity through access to more distal (↑volumetric coverage) and smaller-diameter (↑spatial resolution) vessels.
- What would happen in the case of ultimate success?
  - Unnecessary x-ray catheterizations could be avoided (↑quality of life, ↓$$).
  - Complementary information in one setting.

Whole Heart Coronary MRA

+Ease-of-use
+Volumetric coverage



Sensitivity: 82, Specificity: 91

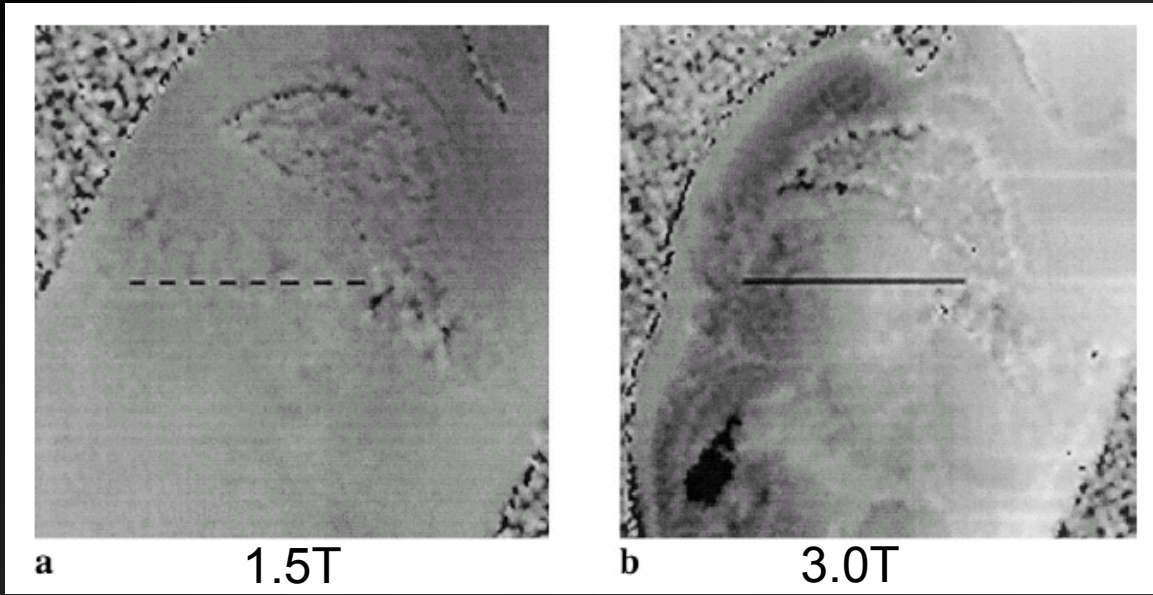
Weber OM. Magn Reson Med. 2003 Dec;50(6):1223-8.

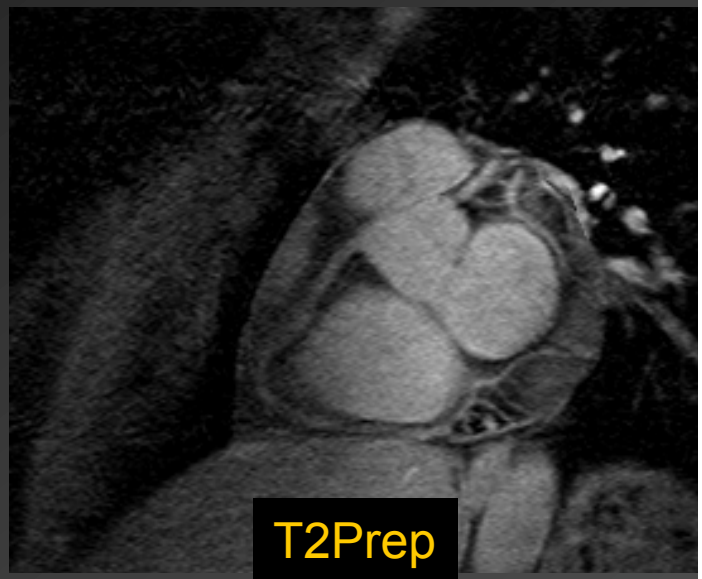
Sakuma H. Radiology 2005;237:316

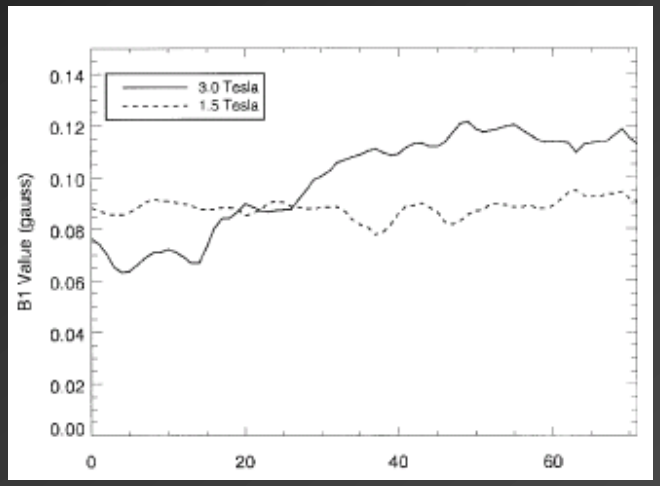
Challenges for CMR @ 3T

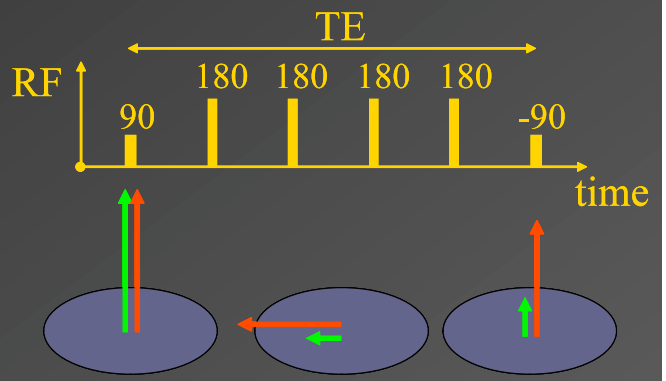
- ECG
  - ↑ magneto-hydro-dynamic effect necessitates modification of ECG hardware & algorithms
- Field inhomogeneity
  - B_0 and B_1
- Patient safety (SAR limitations)
  - ↑ B_0 → ↑ ω_0 → ↑ RF deposition SAR (SSFP →↓RF excitation angles ↓contrast, TSE...)
- Enhanced spatial resolution
  - Need for improved motion suppression

Challenges @ 3T: B_1 Inhomogeneity



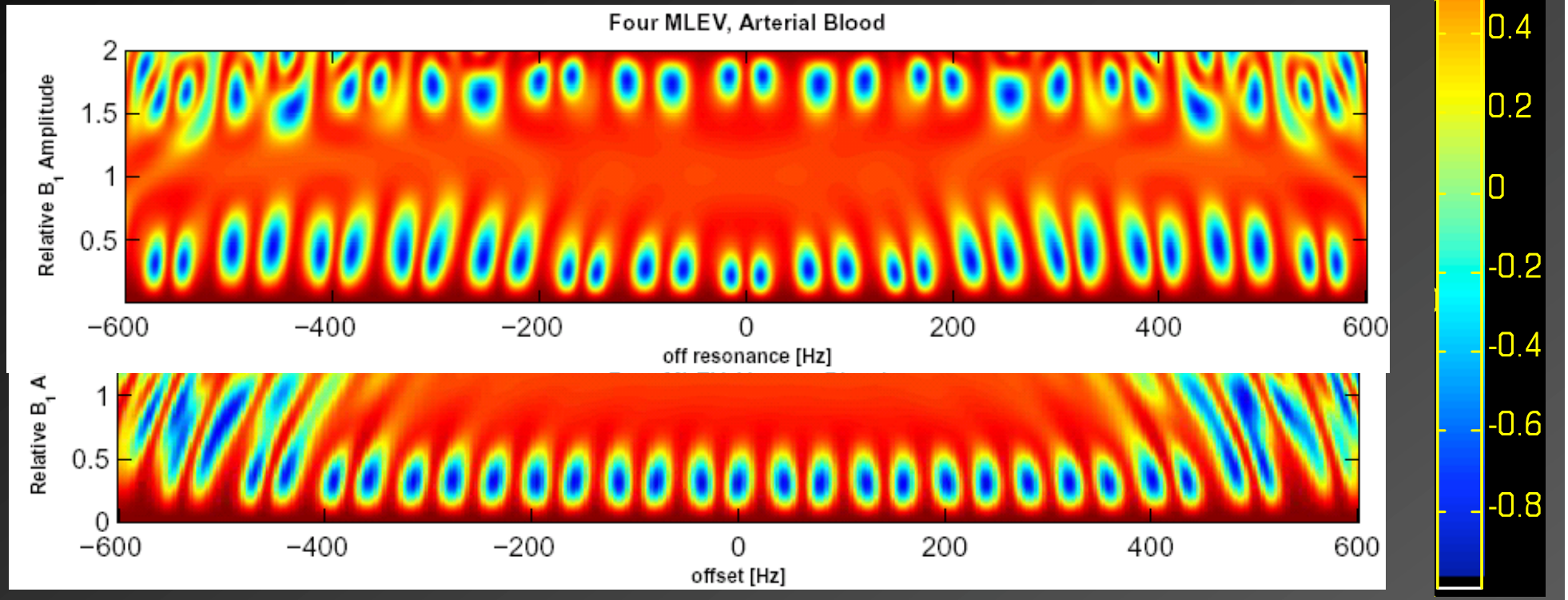






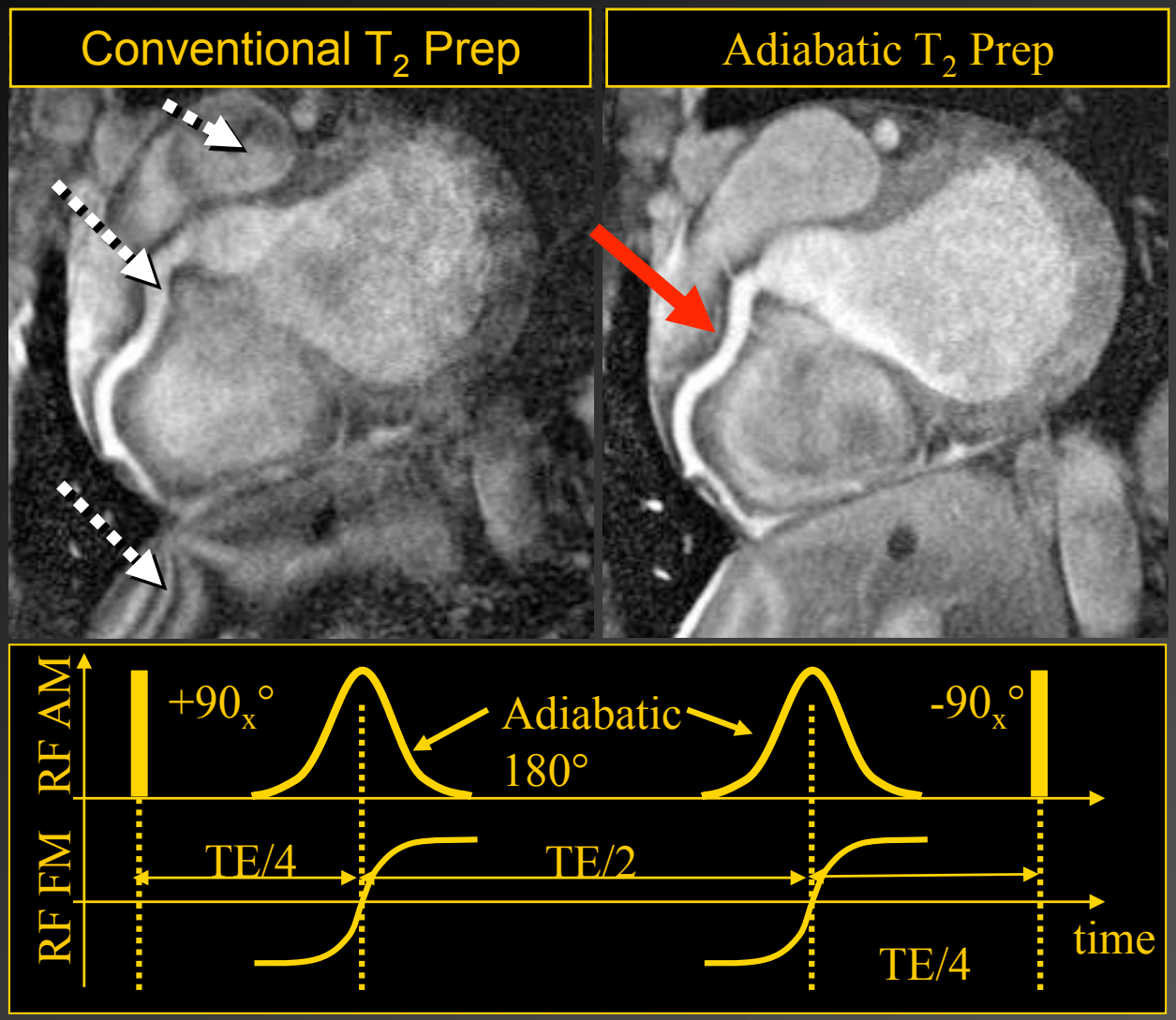
Greenman et al.: JMRI, 2003 Jun;17(6):648-55.

Solutions @ 3T: $\uparrow \Delta B_1 \rightarrow$ *Adiabatic T2Prep*



Nezafat R. Magn Reson Med. 2006 Apr;55(4):858-64.

Solutions @ 3T: $\uparrow \Delta B_1 \rightarrow$ *Adiabatic T2Prep*



Nezafat R., Stuber M. et al.: Magn Reson Med. 2006 Apr;55(4):858-64.

Potential for Coronary MRA @ 3T

(0.34x0.35x1.5mm voxel size)

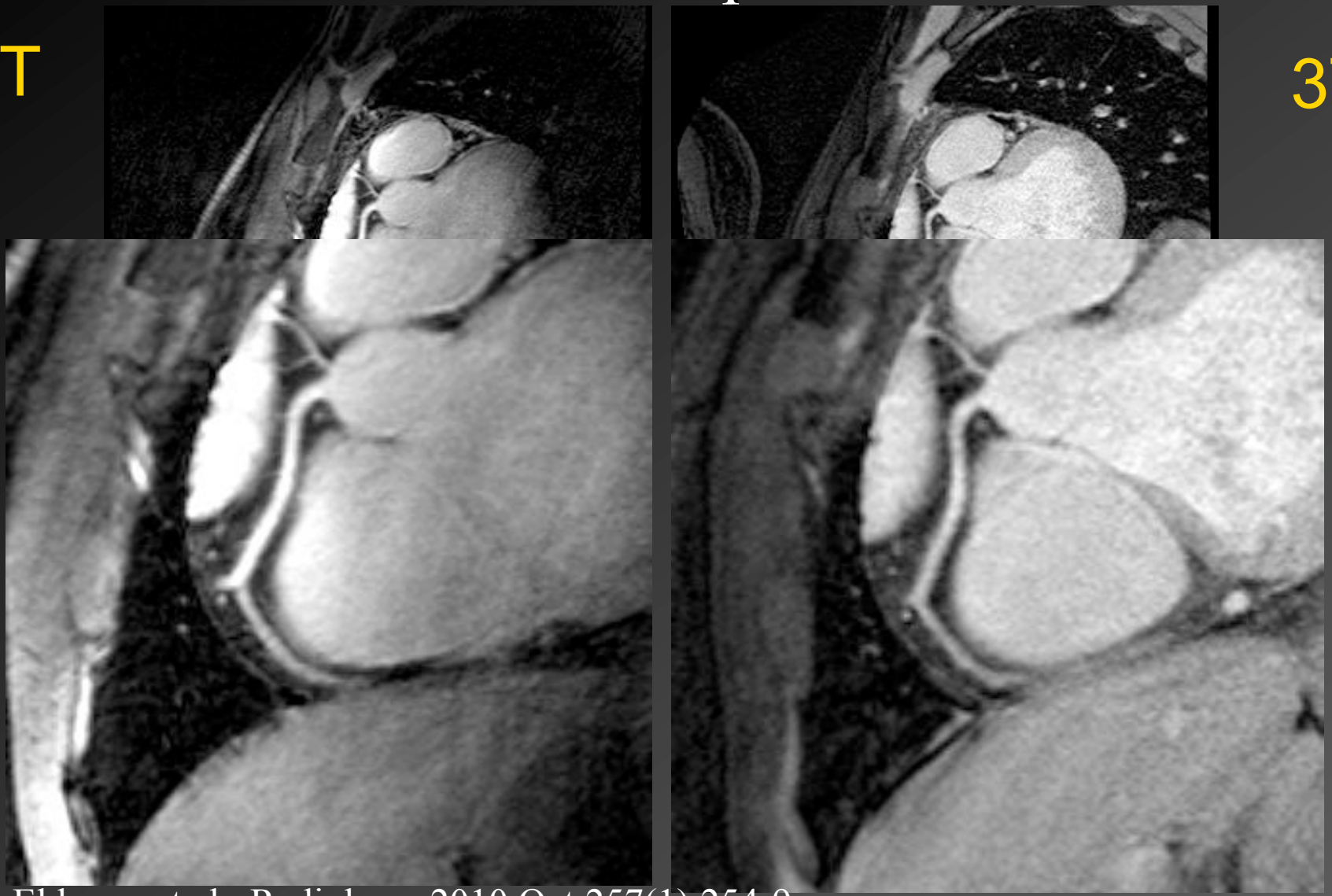
- **MR System**
  - Philips 3T Achieva
  - Dual Quasar Gradient System
  - 6-Element Cardiac SENSE Coil
- **Imaging Sequence**
  - 3D TFE (volume targeted, 2cm)
  - TE/TR: 2.3/7.6ms
  - Matrix/FOV: 800/270mm
  - Acquired Voxel Size: 0.34x0.35x1.5mm
  - Reconstructed Voxel Size: 0.26x0.26x0.75mm
  - Fat Saturation
  - 2nd Order Shimming
  - Scanning time ~10min
- **Motion Suppression**
  - *FREEZE* (automated prescription of diastolic rest period)*
  - VECG
  - Free-Breathing & Real-Time Navigator

*Ustun A. et al.: *AJR* 2007

High Field Coronary MRA (7T)

First Steps…

7T

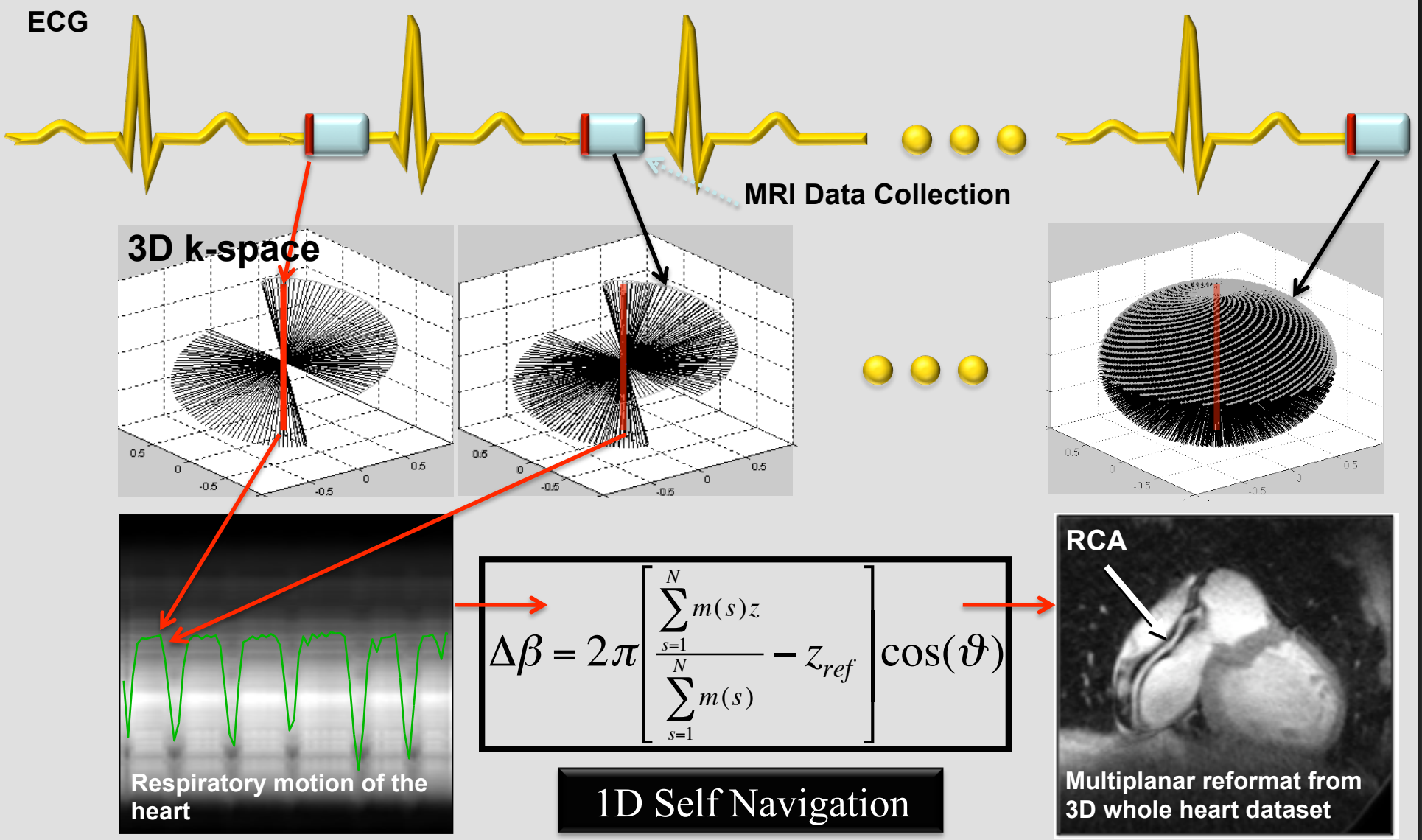


3T

S. van Elderen, et al.: Radiology. 2010 Oct;257(1):254-9.

Self-Navigated Whole Heart MRI

Stehning C. et al.: *Magn Reson Med*. 2005 Aug;54(2):476-80

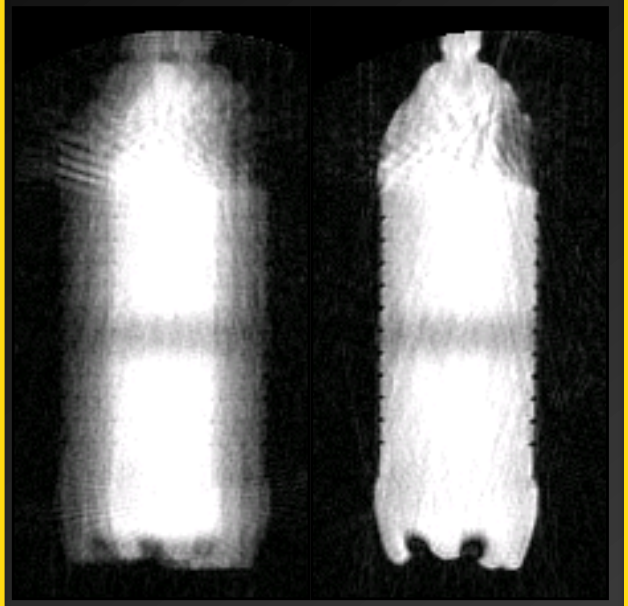


Self-Navigated Whole Heart MRI

Stehning C. et al.: *Magn Reson Med*. 2005 Aug;54(2):476-80
Piccini D. et al.: *Magn Reson Med*. 2011 Apr 5.

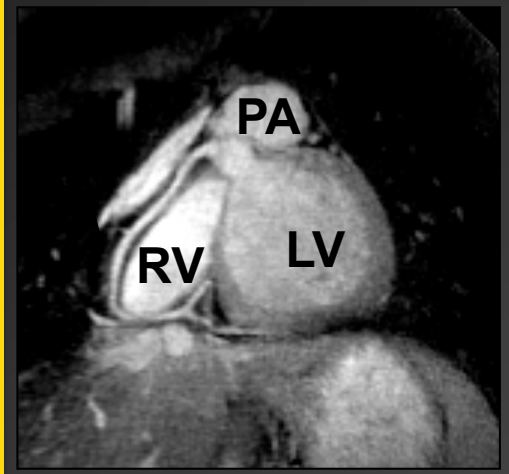
In Vitro Moving Phantom

Un-corrected self-navigated



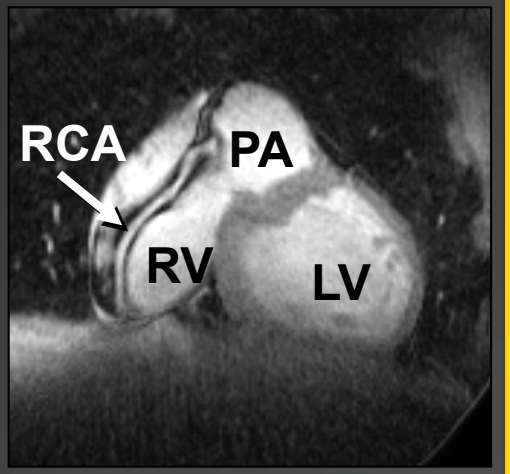
In Vivo 3D Whole Heart Human Data

navigator (conventional)



Localizers	**2**
Scan time	**16 min**
Efficiency	**50%**

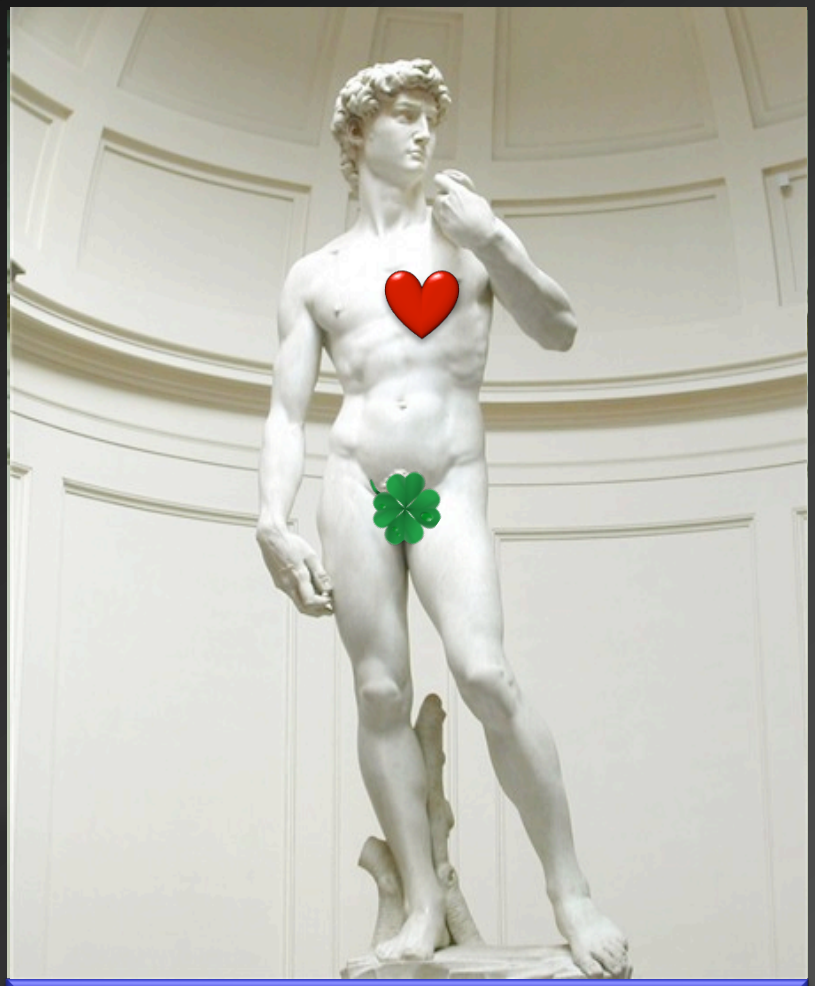
self-navigated



Localizers	**1**
Scan time	**8 min**
Efficiency	**100%**

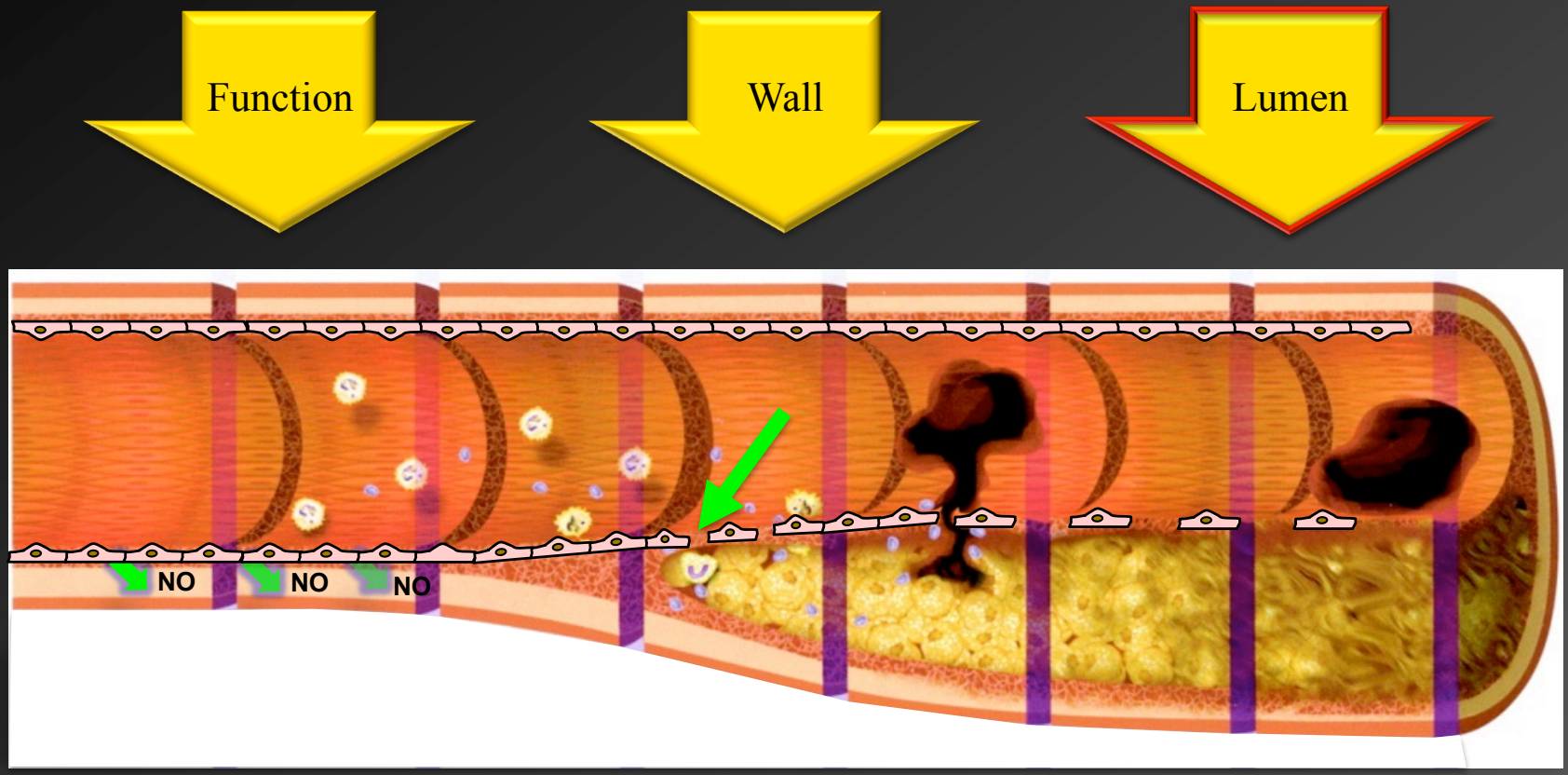
- ↑Time efficiency
- ↑Ease-of-use
- Potential for ↑quality motion of correction

Societal changes and risk factors: Early Atherosclerosis



David, 1504, ca 20 years

Progression of Coronary Atherosclerosis

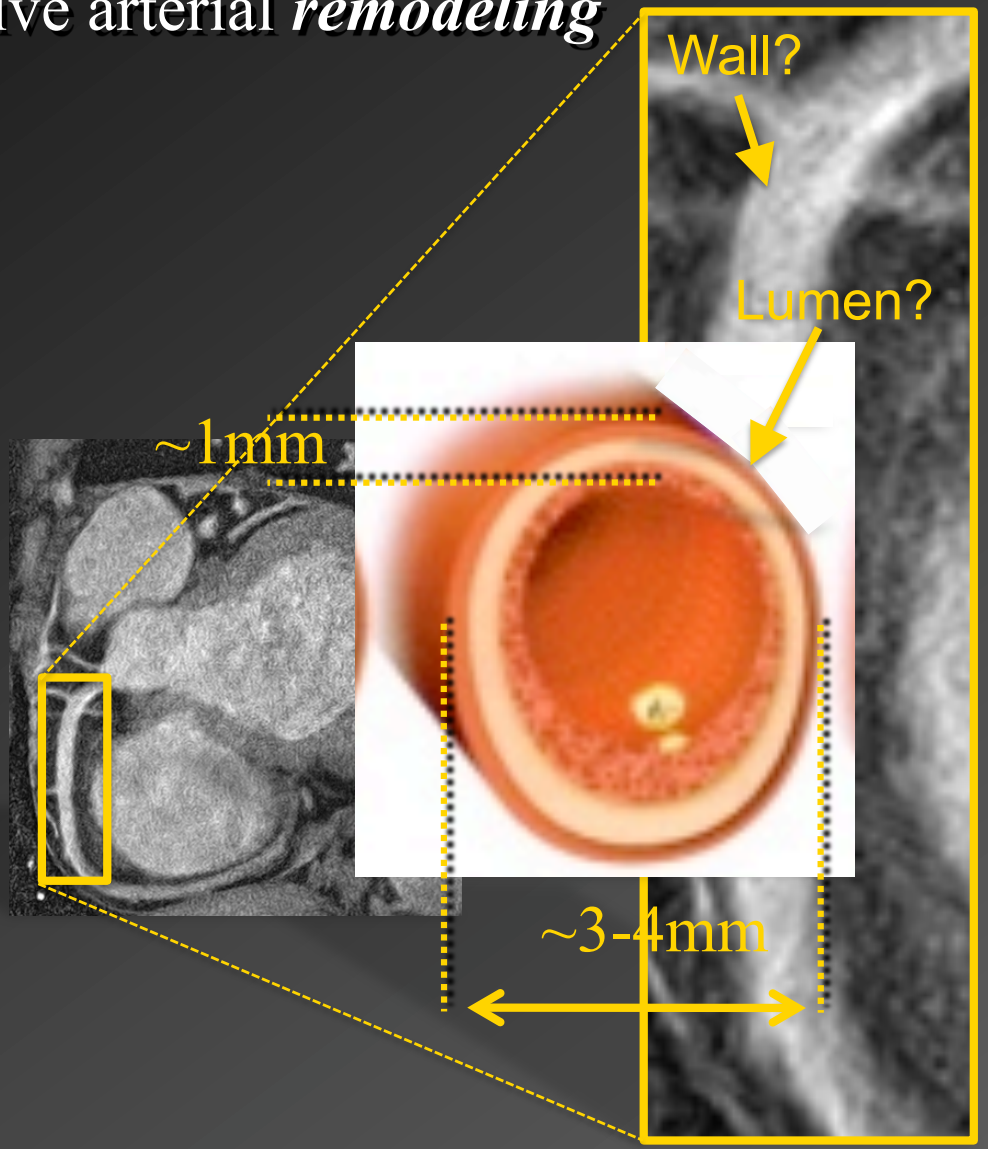


Adapted from Libby Circulation 2001;104:365-72

Hypothesis: The coronary vessel wall can be visualized non-invasively using MRI for the ***quantitative characterization*** of ***early atherosclerotic*** positive arterial ***remodeling***

Challenge:

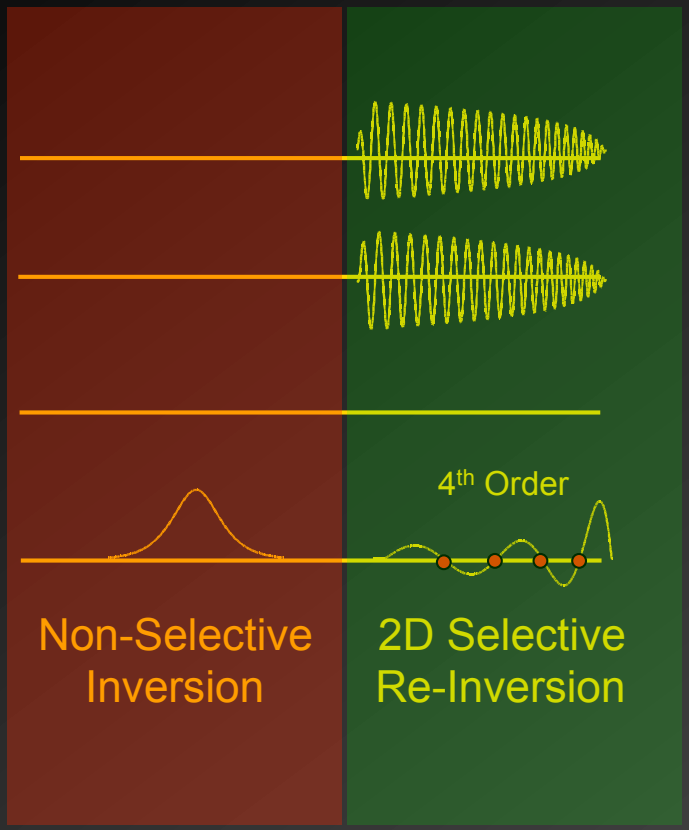
- *Small dimensions*
- *Motion*
- *Contrast*
  - *Wall*
  - *Lumen (blood)*

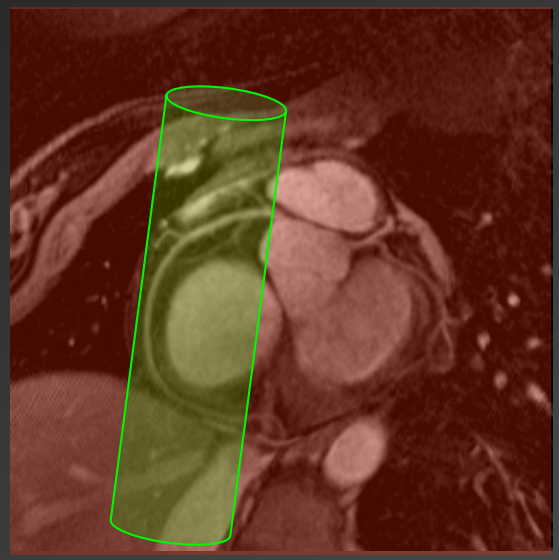


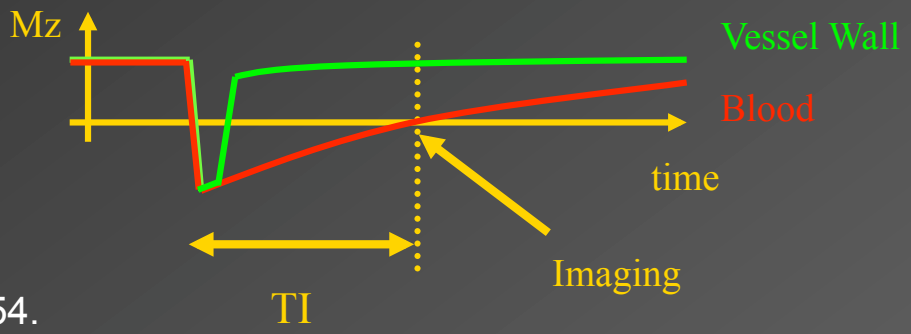
Generation of Contrast

	T1 [ms]	T2 [ms]	$\Delta\omega_0$ [Hz]	flow
Blood	1650	250	0	yes
Muscle	1200	50	0	no
Fat	300	100	440	no

Local Inversion[1]

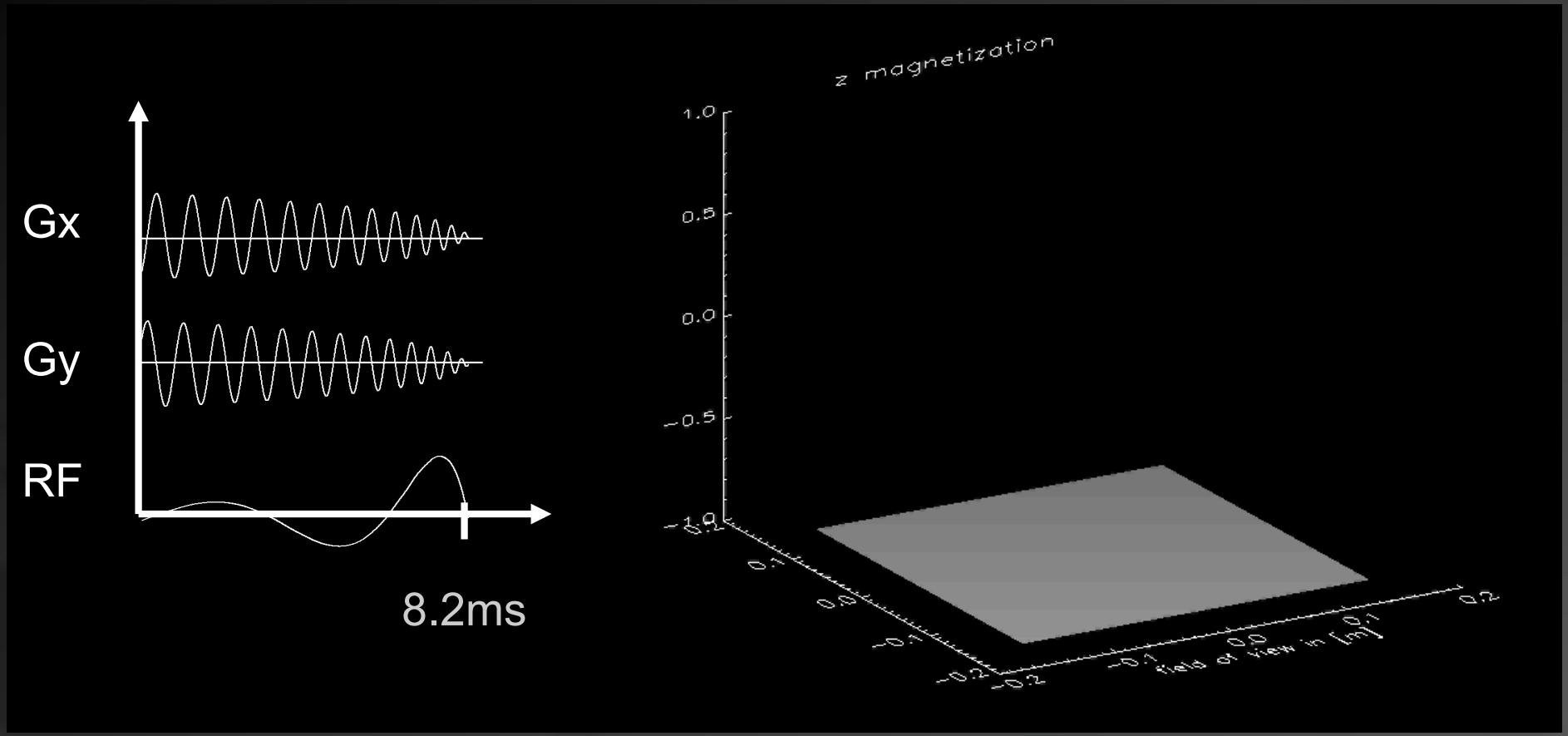






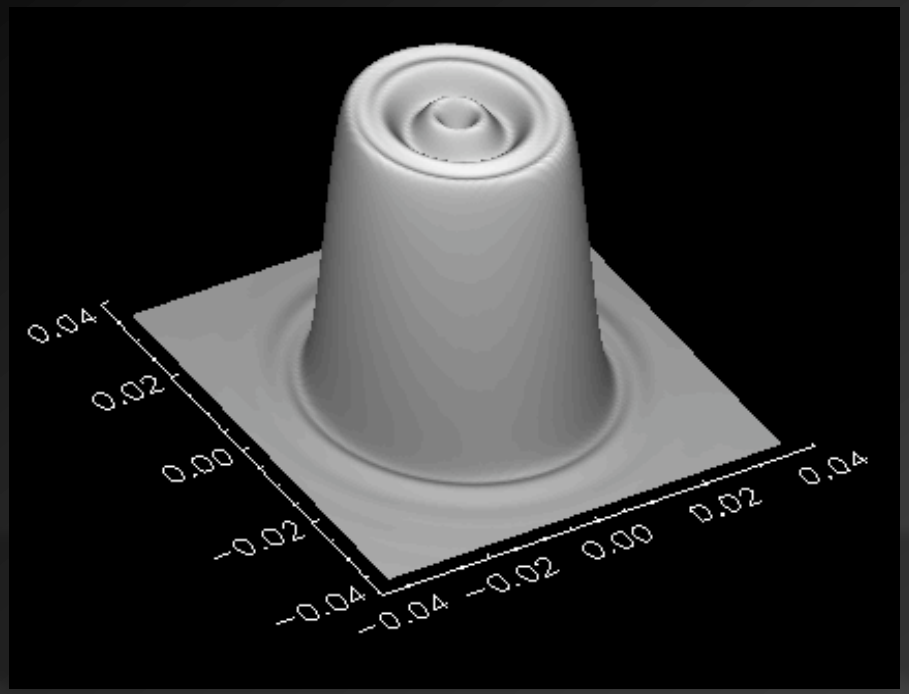
1) Botnar et al.: Magn Reson Med. 2001 Nov;46(5):848-54.
2) Edelman RR, Chien, D, Kim D: *Radiology*; 181(3); 655-660 (1991).

Design of a Cylindrical Pulse*

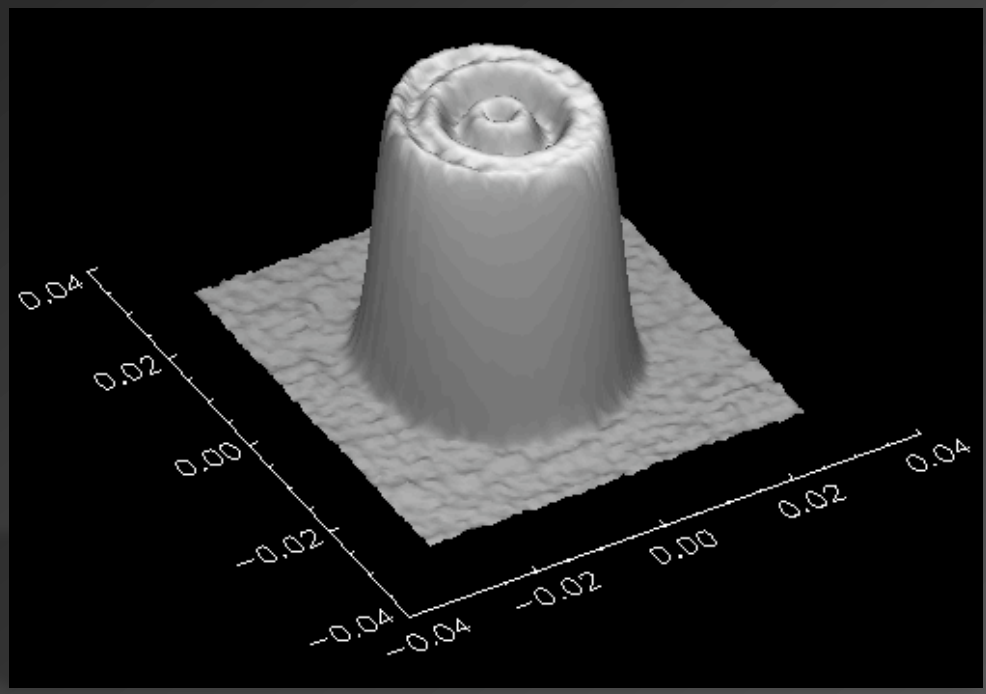


* Diploma Thesis C. Barmet, ETHZ

Design of a Cylindrical Pulse*



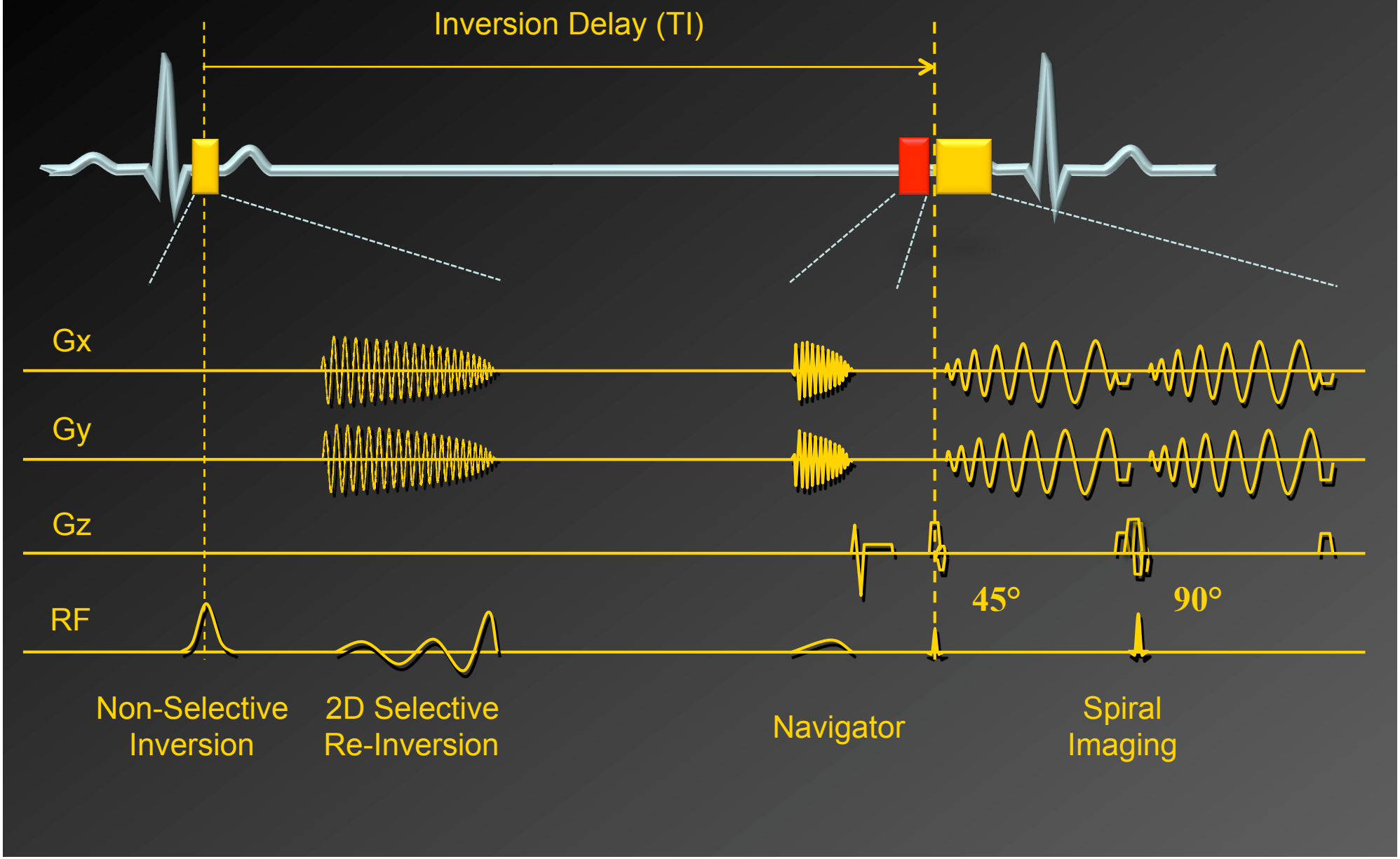
Numerical Simulation



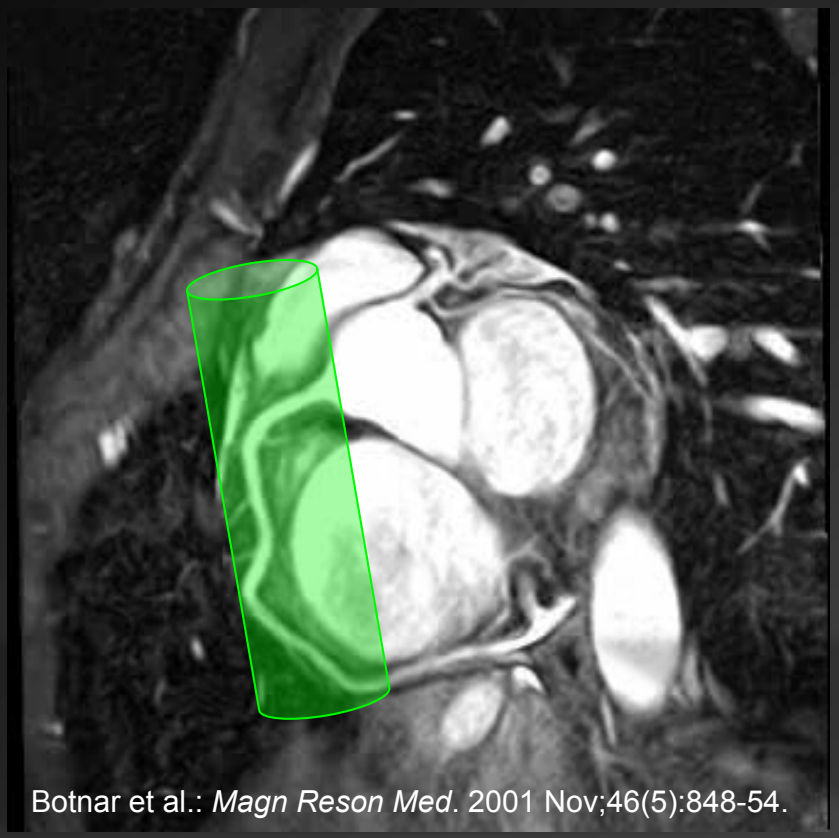
Phantom Experiment

* Diploma Thesis C. Barmet, ETHZ

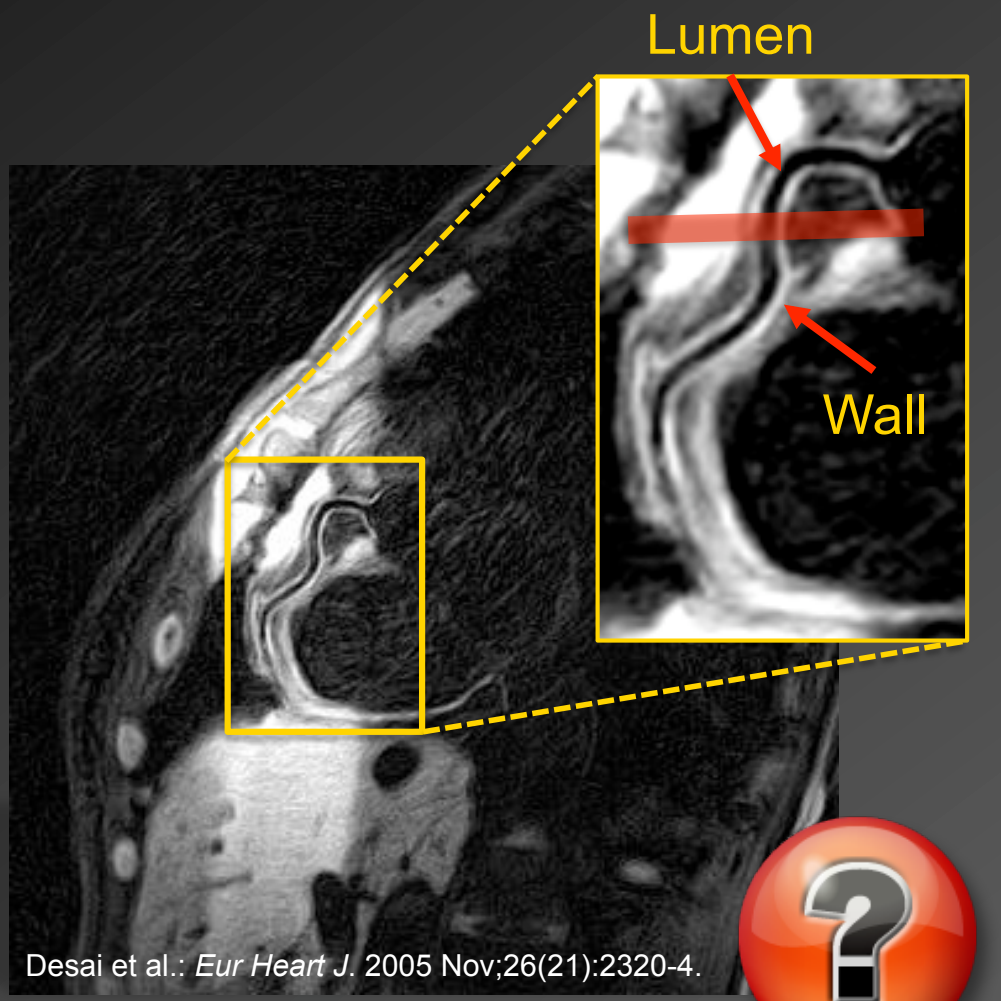
Coronary Vessel Wall Imaging



Coronary Vessel Wall Imaging



Botnar et al.: *Magn Reson Med*. 2001 Nov;46(5):848-54.

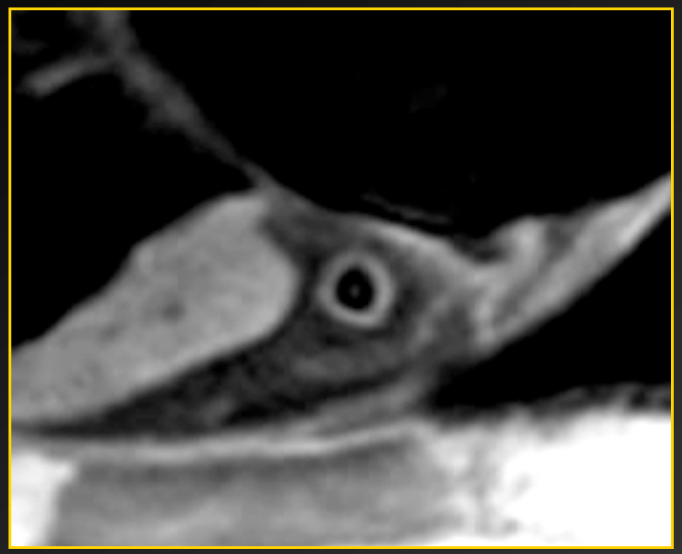


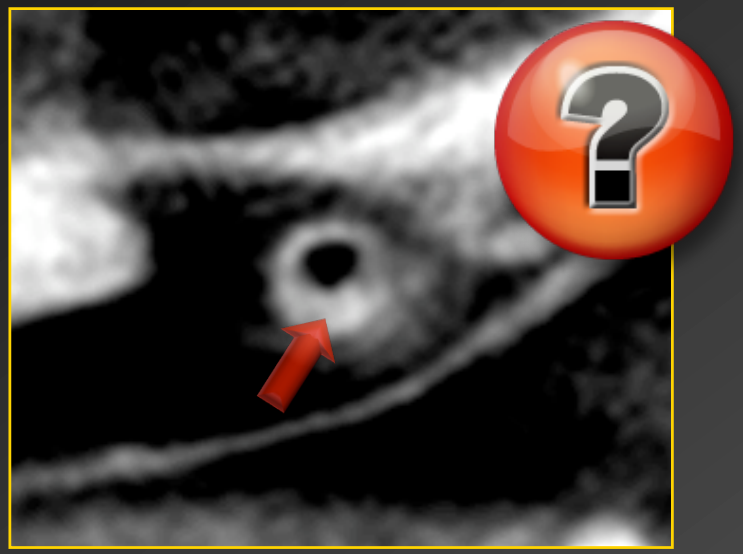
Desai et al.: *Eur Heart J*. 2005 Nov;26(21):2320-4.

Coronary MRA

MRI of the vessel wall

Coronary Vessel Wall Imaging



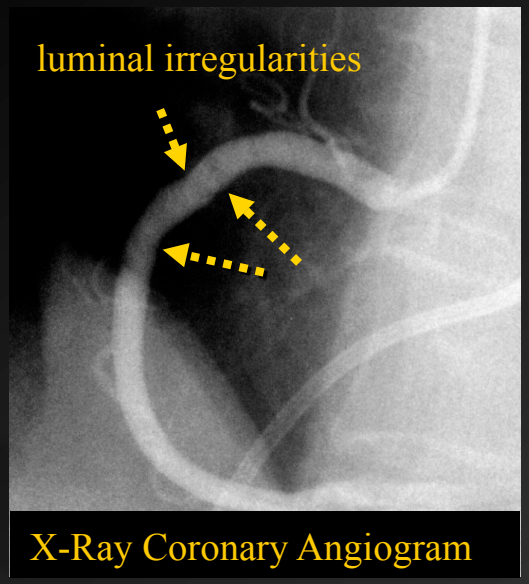


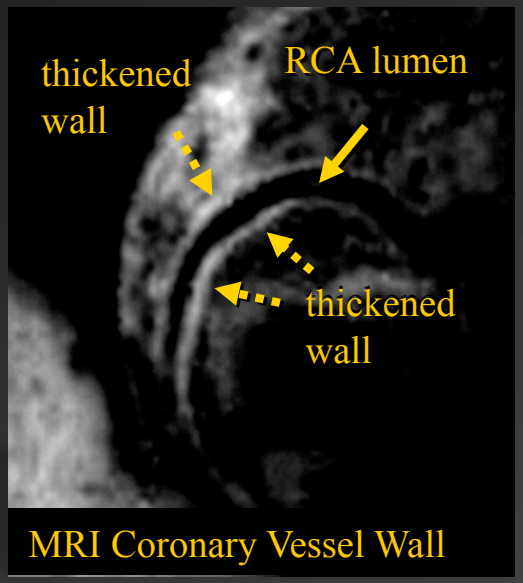
HEALTHY

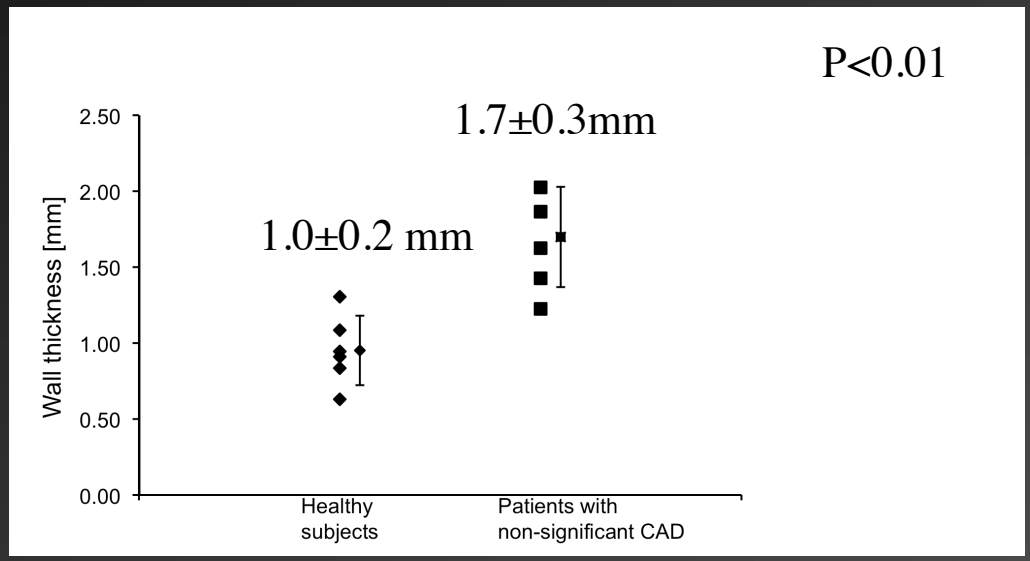
PATIENT

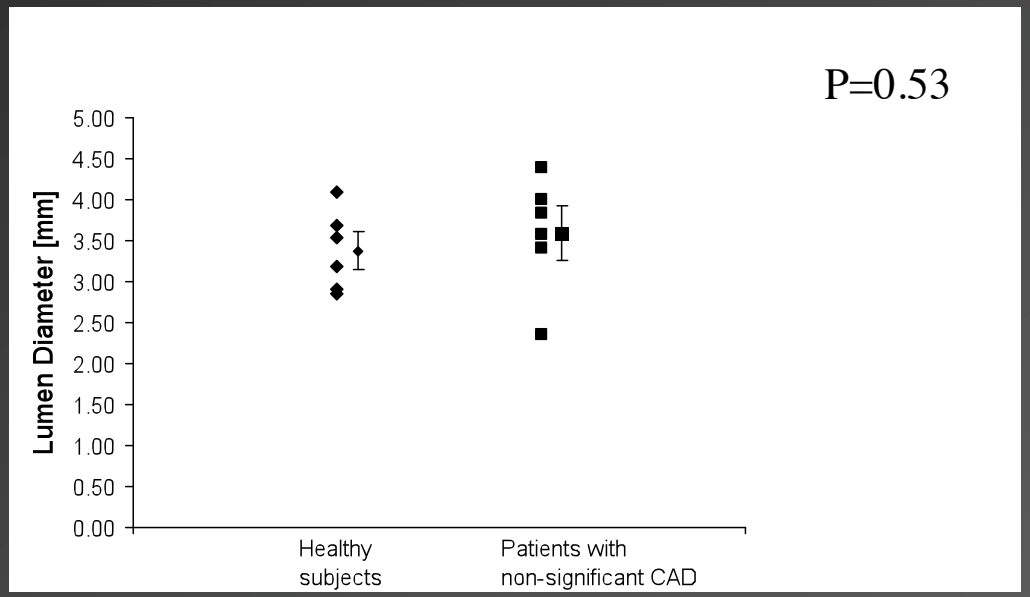
Hays A. et al.: Submitted *AHA* 2010

Coronary Vessel Wall Thickness



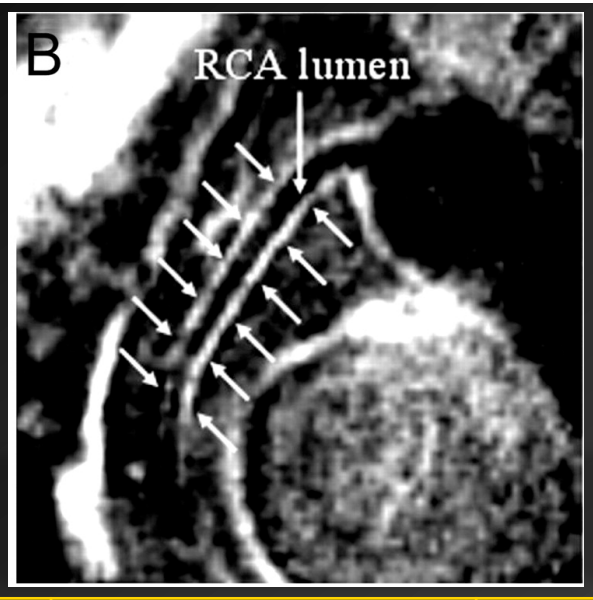


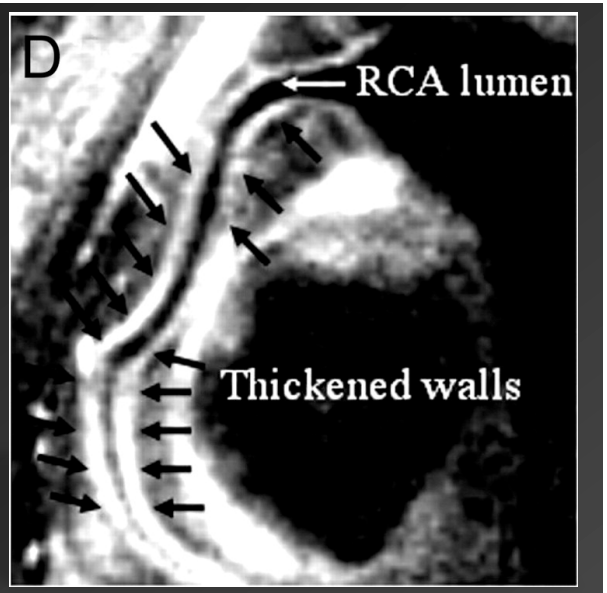




* Kim W, Stuber M, Manning WJ et. Al.: *Circulation* 2002

Coronary Vessel Wall MRI: Current State of the Art

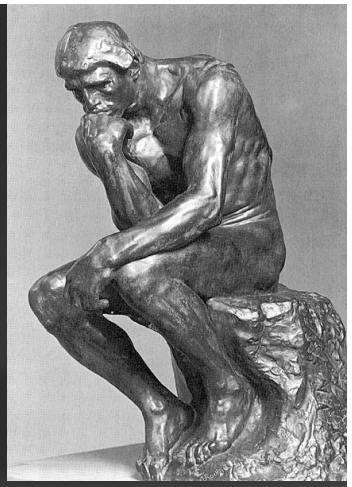




	Subjects With Normoalbuminuria (N=37)	Subjects With Diabetic Nephropathy (N=24)	*P*
RCA interpretable, n (%)	33 (89)	21 (88)	0.8
RCA VW image quality	3.2±0.9	2.9±0.7	0.2
RCA VW mean thickness, mm	1.3±0.2	1.7±0.3	<0.001
RCA VW maximum thickness, mm	1.6±0.3	2.2±0.5	<0.001
RCA plaque detected, n (%)	5 (15)	16 (76)	<0.001
VW indicates vessel wall. Data are mean±SD when appropriate.			

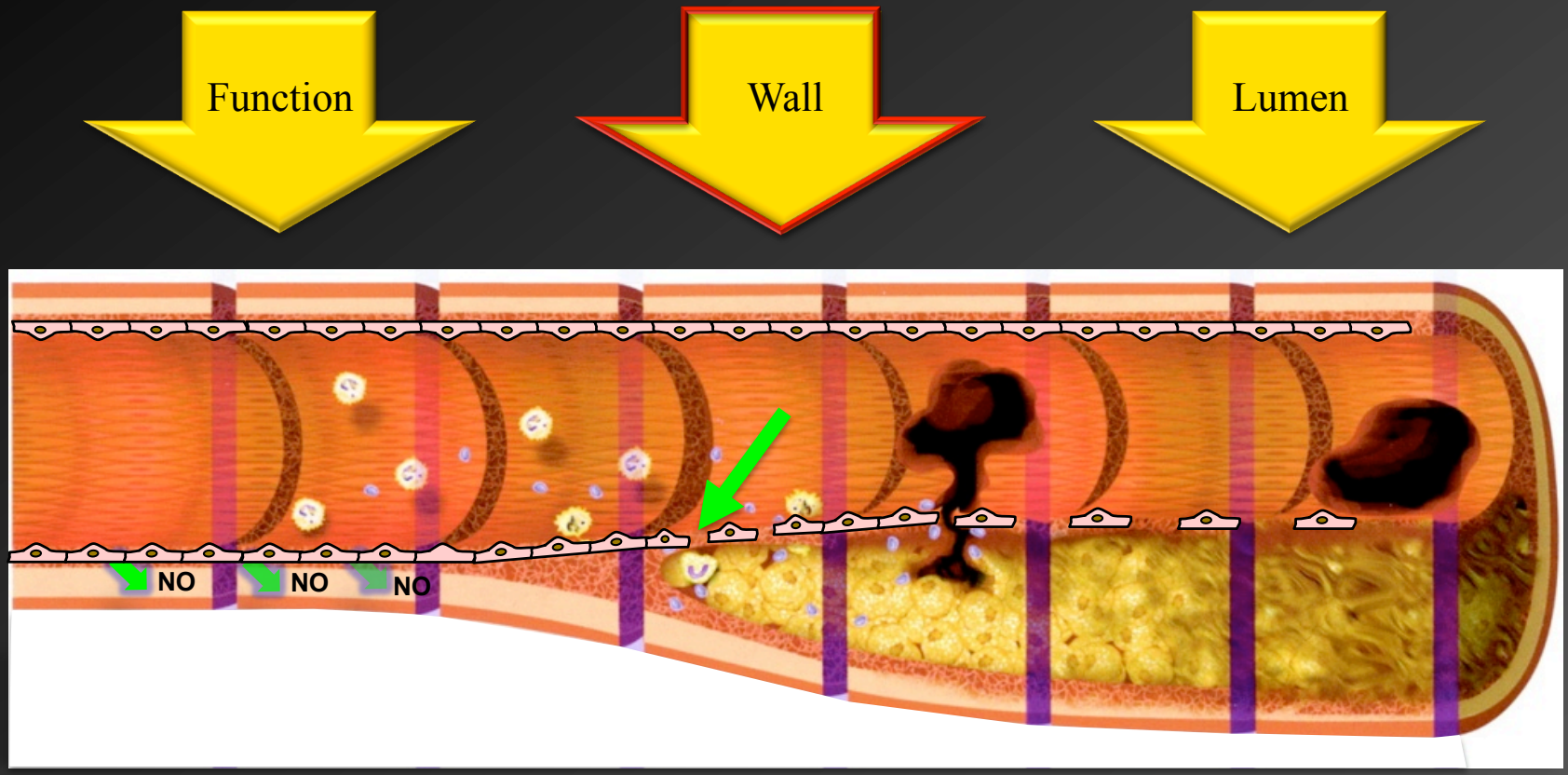
Kim WY et al.: Circulation. 2007 Jan 16;115(2):228-35

Time to Reflect…



- What have we learned?
  - Sophisticated MRI methods enable the non-invasive identification and quantification of early atherosclerotic positive coronary arterial remodeling.
- What is needed to take this to the next level?
  - IVUS correlation.
  - Ability to differentiate different plaque components.
- What would happen in the case of ultimate success?
  - Plaque that is prone to rupture can be identified non-invasively.

Progression of Coronary Atherosclerosis



Adapted from Libby Circulation 2001;104:365-72

Stem Cells and MRI

- Cells are MR ‘invisible’: → iron (Fe) labeling* (↑susceptibility)
  - Monitoring of delivery
  - Visualization of migration
  - Determination of fate
  - Quantification of function

Kraitchman, Bulte et al.: Circulation 107(18), 2003

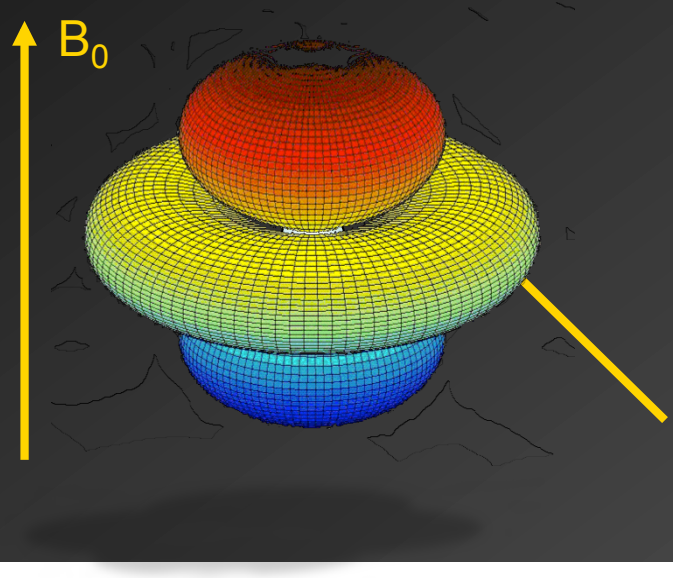
Stem Cells and MRI

- Problem:
  - Negative contrast from susceptibility artifacts are difficult to discriminate from other potential sources of signal voids absence of tissue, motion artifacts, calcifications, water/fat out of phase etc.
- Objective:
  - The development of an MRI methodology that enables the *signal-enhanced* visualization of iron labeled stem cells.

Design of a Positive Contrast MRI Method

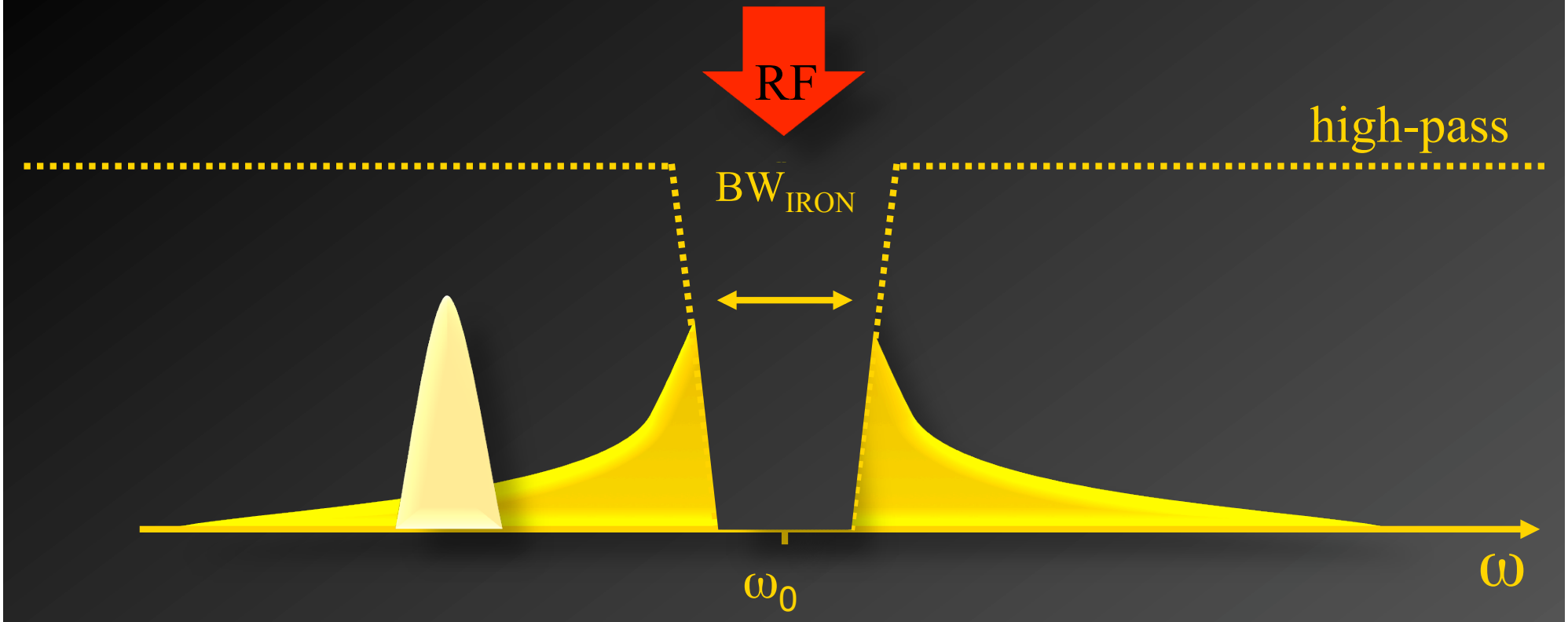
- Superparamagnetic material → local magnetic field change → frequency shift:

$$\Delta B(r,\Theta)_{External} \sim \frac{\Delta K}{3}\frac{a^3}{r^3}\left(3\cos^2\Theta - 1\right)B_0$$



$$\Delta\omega = \gamma\Delta B(r,\Theta)_{External}$$

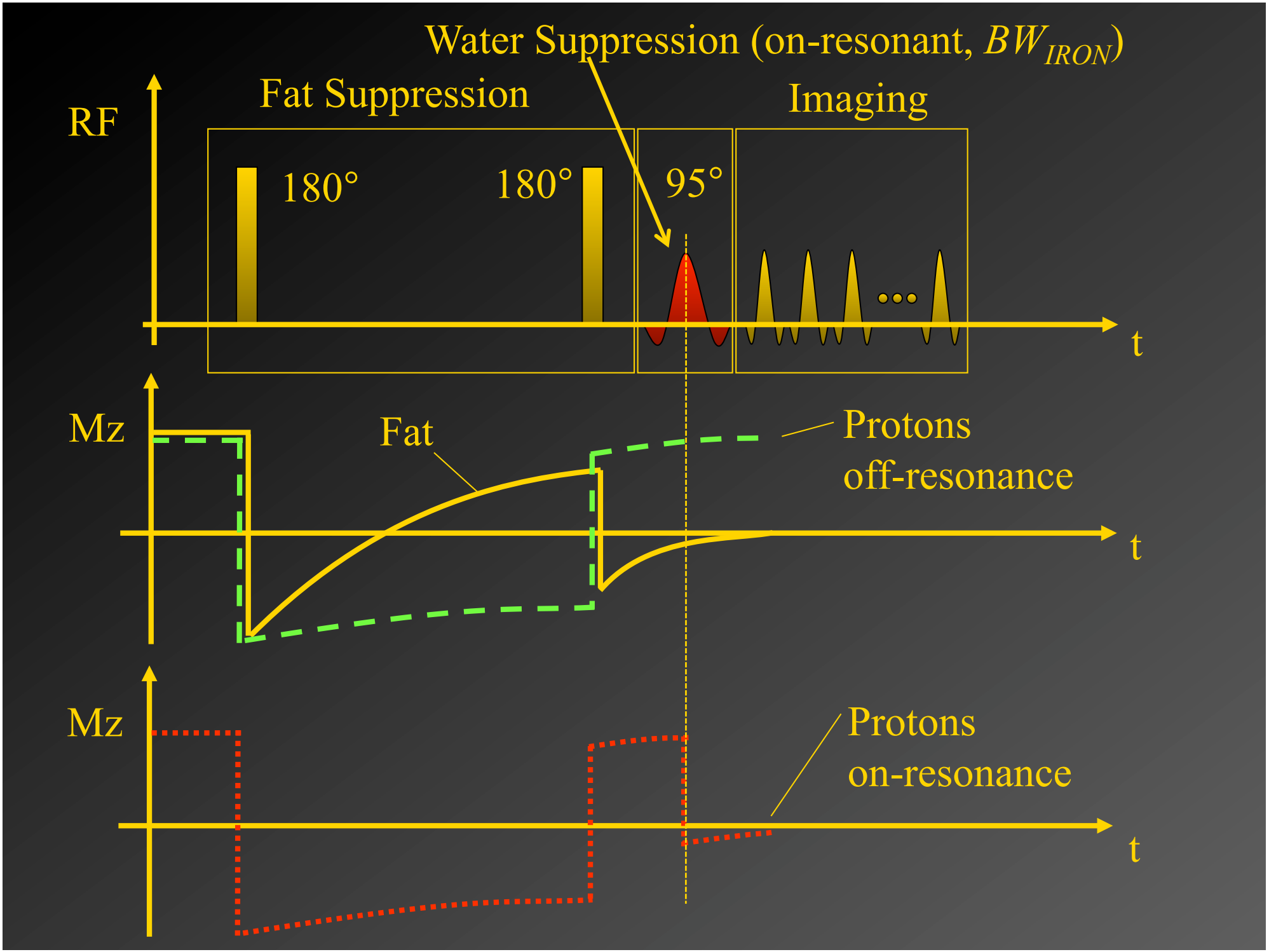
Design of a Positive Contrast MRI Method



Fat

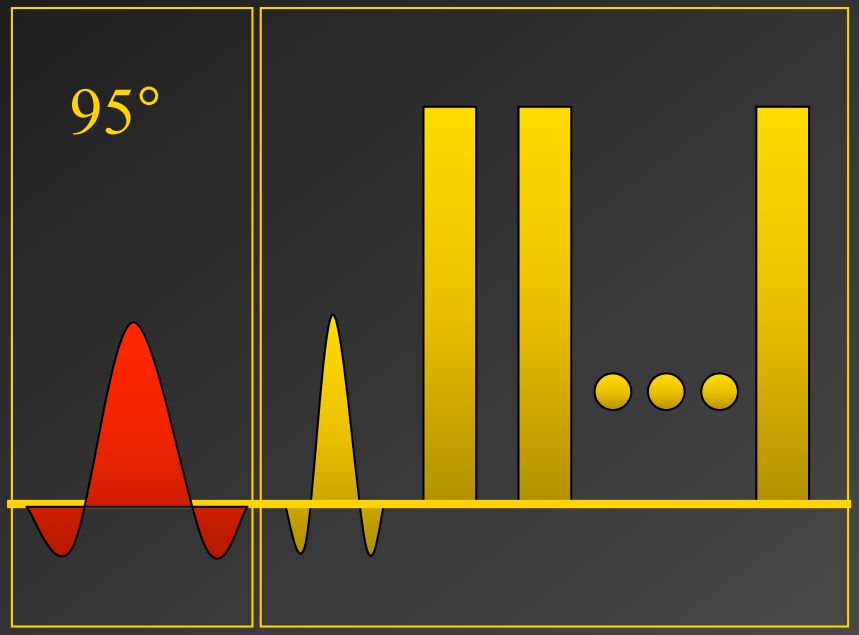
Protons on-resonance

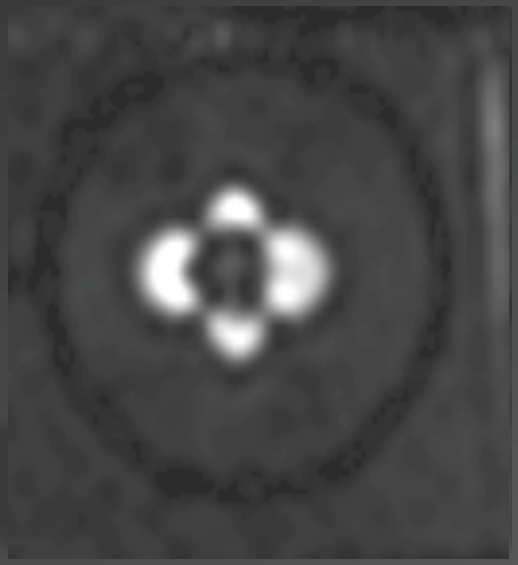
Protons off-resonance

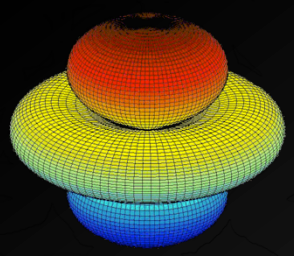

Water Suppression (on-resonant, BW_{IRON})
Fat Suppression
Imaging
RF
180°
180°
95°
...
t
Mz
Fat
Protons
off-resonance
t
Mz
Protons
on-resonance
t

Visualization of Iron Labeled Stem Cells with Positive Contrast

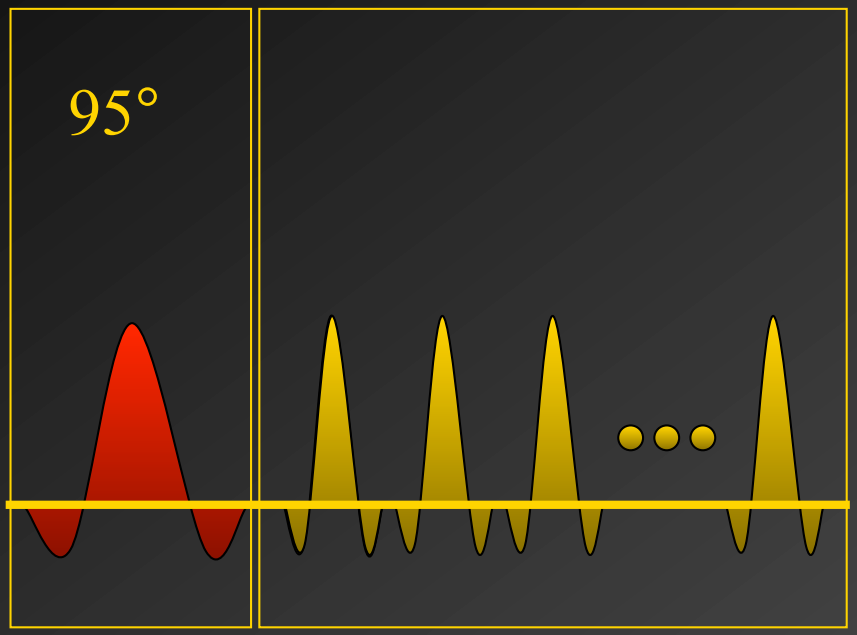
- In vitro experiment 3T:
  - Water suppression

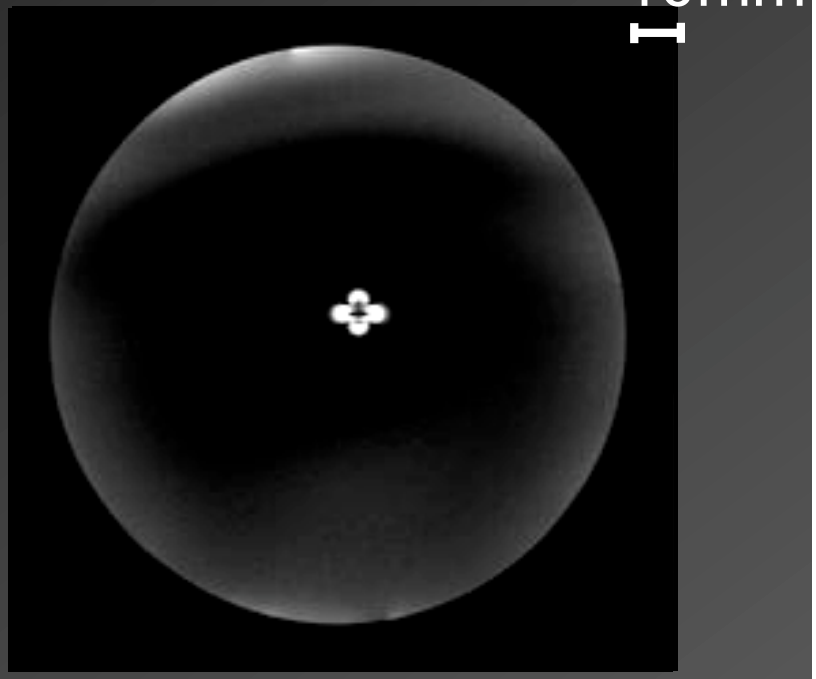






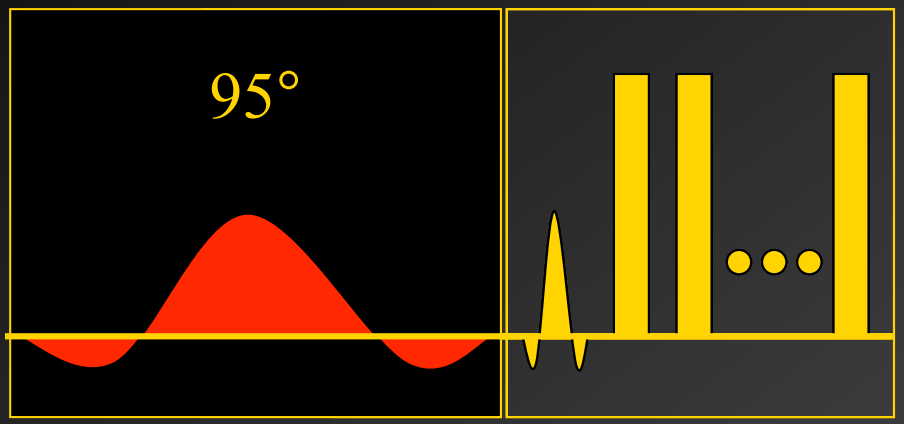
IRON Imaging

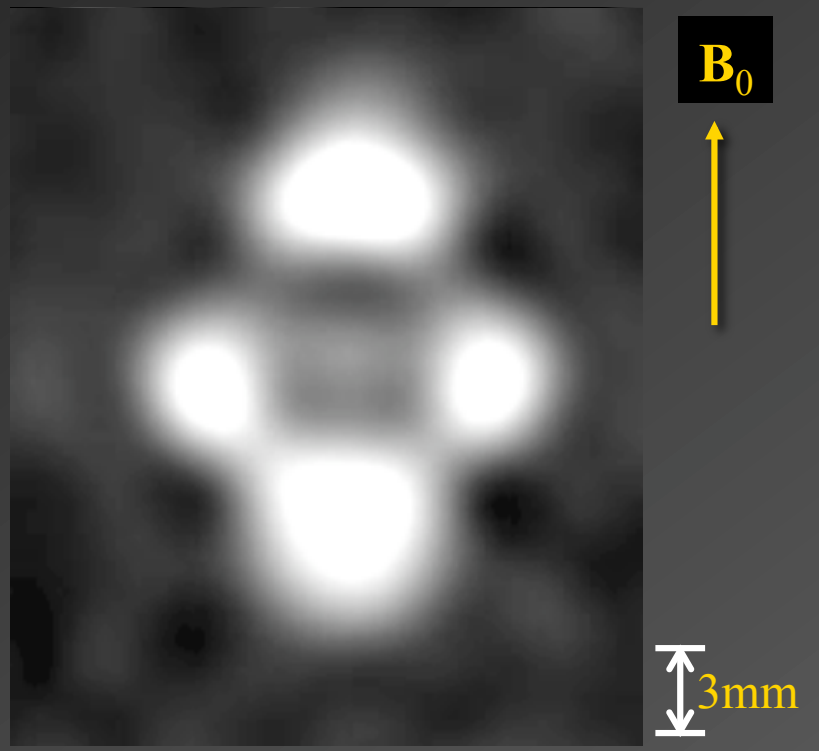




Results:

IRON* Imaging (1.5T) : *Adjustment of Sensitivity*





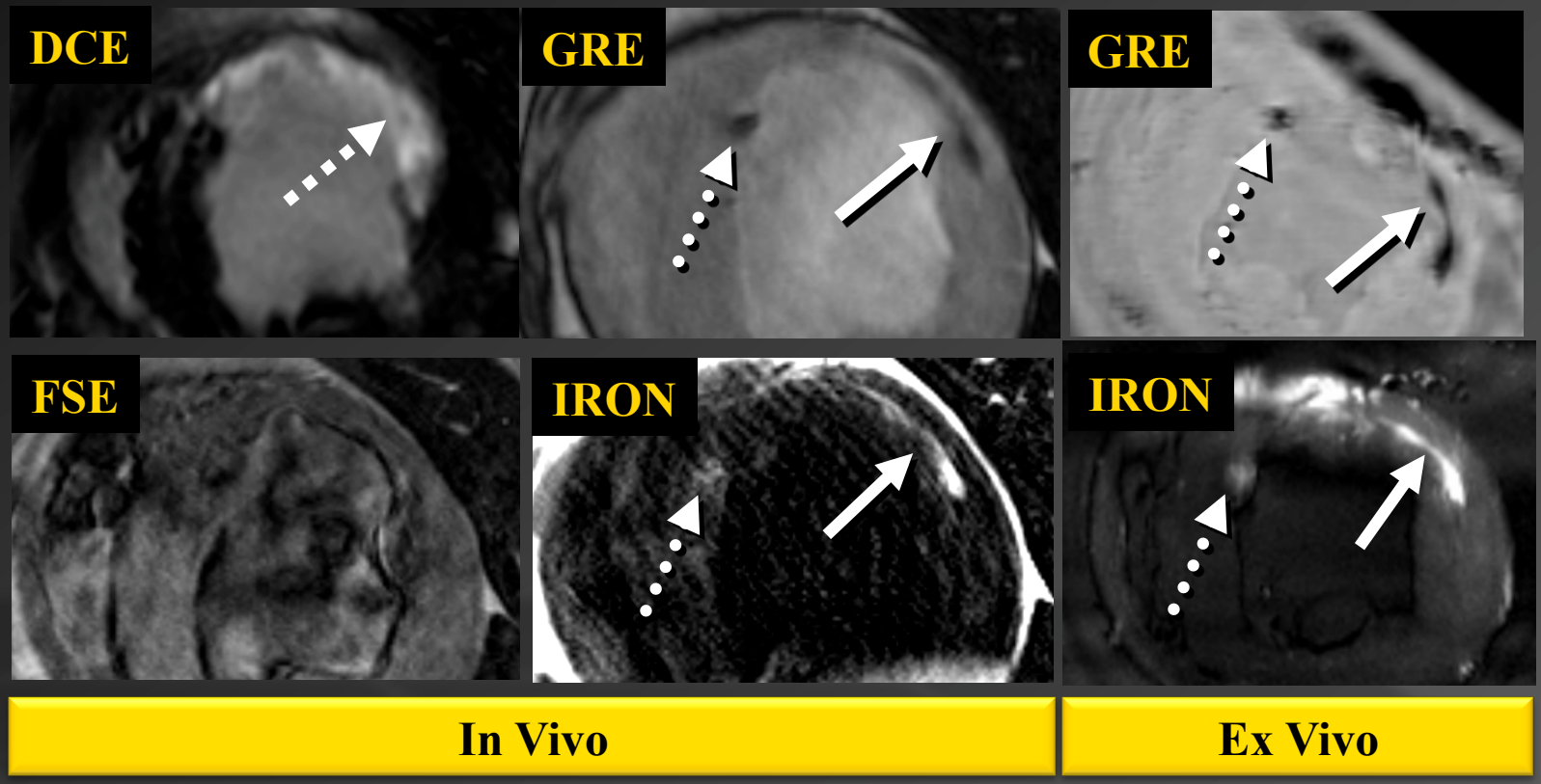
BW_{Water}=100Hz

*Stuber M. et al.: *Magn Reson Med*. 2007 Nov;58(5):1072-7.

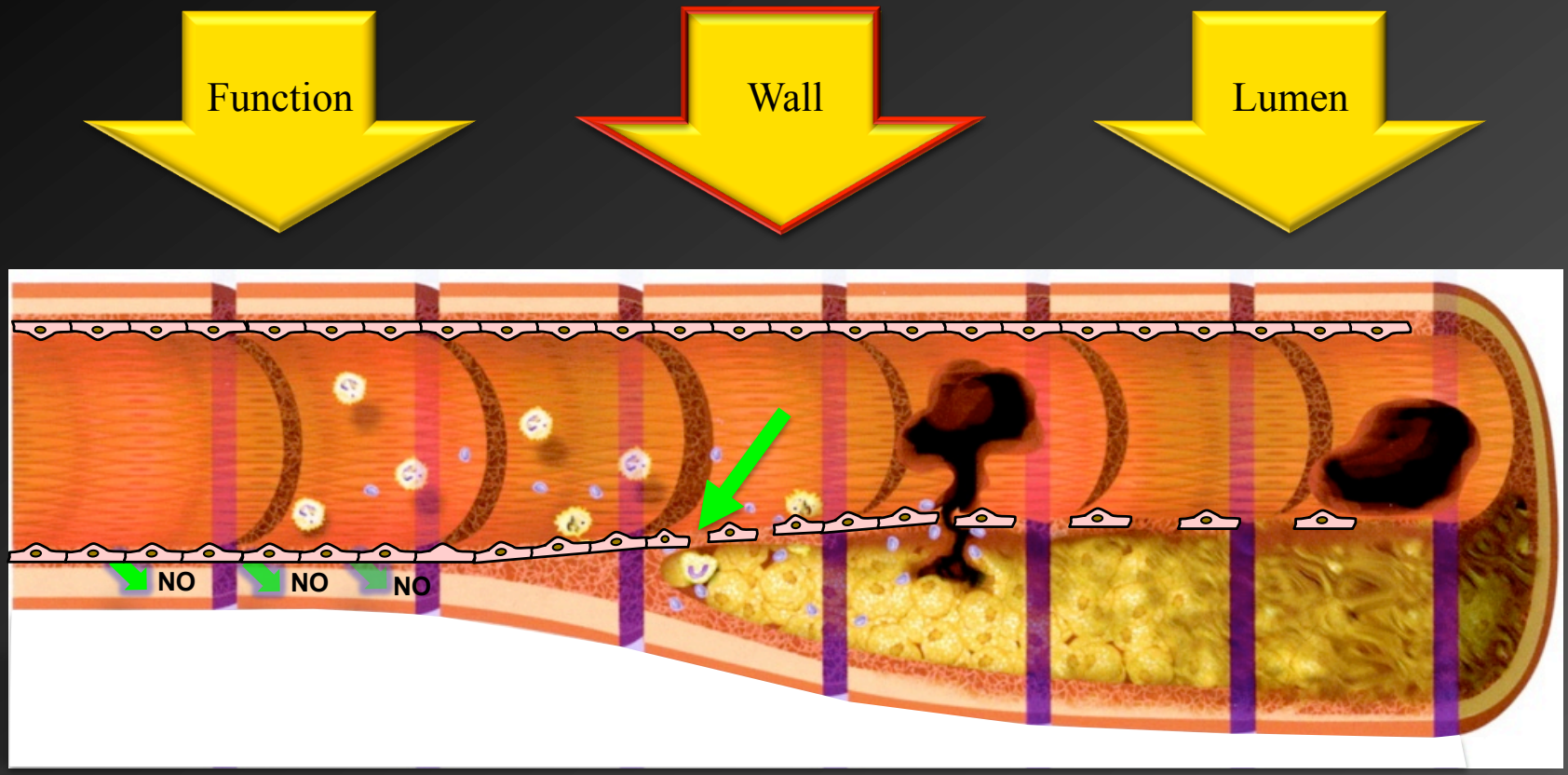
Visualization of Iron Labeled Stem Cells with Positive Contrast

- In vivo cardiac imaging:
  - Stem cell injection into infarcted dog heart

$0.6 \times 0.6 \times 2 mm^3$



Progression of Coronary Atherosclerosis



Adapted from Libby Circulation 2001;104:365-72

“Molecular” Imaging

- Vulnerable plaque[1]
  - Inflammation[2,3] → recrutment of monocytes or macrophages.[4]

- Iron oxide nanoparticles

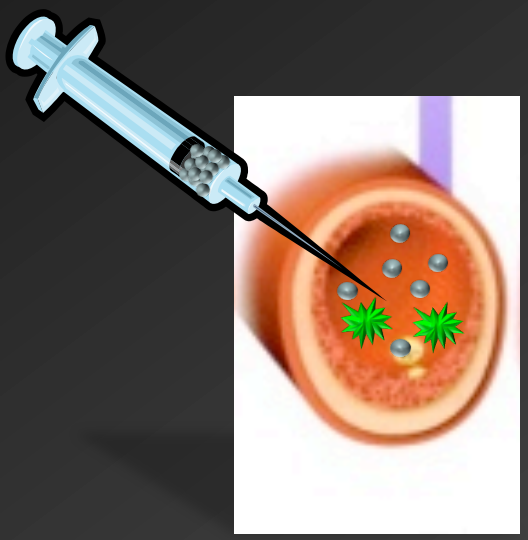
  - Macrophages: Phagocytosis of such nanoparticles.

1) Naghavi et al.: *Circulation*. 2003;108:1664-72.
2) Swirski et al.: *Proc Natl Acad Sci U S A*. 2006;103:10340-5.
3) Libby: *Nature*. 2002;420:868-74.
4) Swirski et al.: *J Clin Invest*. 2007;117(1):195-205.

*Kindly provided by Ralph Weissleder, MGH Boston.

The Trojan Horse

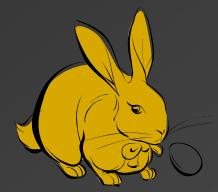
- Intravenous injection of nanoparticles*.
- Macrophages → 1.) phagocytose those nanoparticles.
  → 2.) accumulate in the vulnerable plaque.
- Hypothesis: Nanoparticle uptake in the vunerable plaque can be visualized with positive contrast IRON imaging.



Domenico Tiepolo, 1773

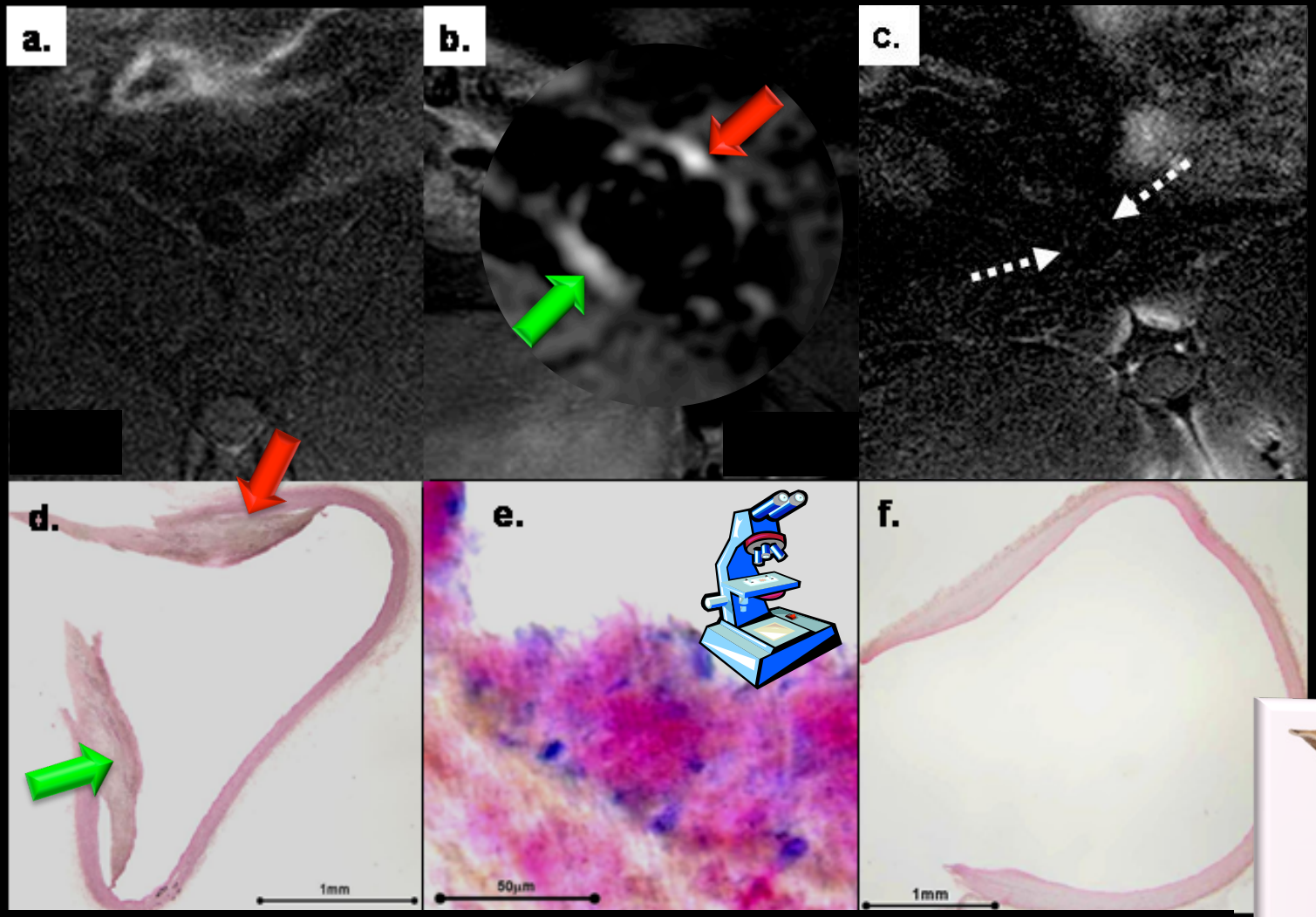
Methods

- Animals:
  - 7 Watanabe (heritable hyperlipidemic) rabbits
    - high-cholesterol diet for 6 weeks
  - 4 New Zealand White rabbits (controls)
    - normal rabbit chow
- Magnetic nanoparticles[1,2]:
  - Monocrystalline iron oxide (↓T2*, T1)
    - (MION)-47 (CMIR, Harvard Medical School)
    - Ø 27.5±6.8nm
    - Plasma half-time 11.4±0.6h (in mice)
    - 250µmol Fe/kg per injection



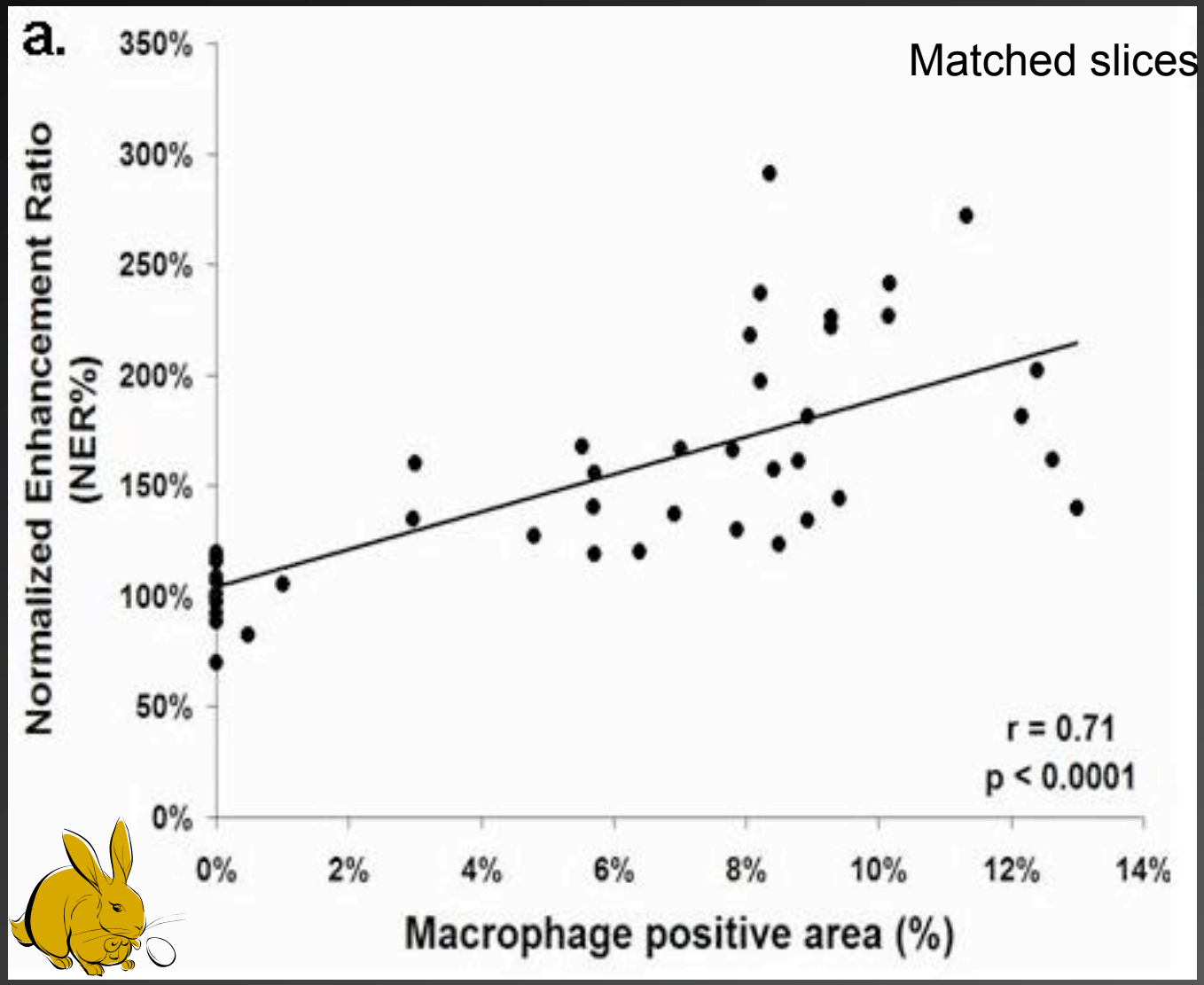
1) Shen et al.: Magn Reson Med1993;29:599-604.
2) Wunderbaldinger et al.: Bioconjug Chem. 2002;13:264-8.

Molecular MRI of Vulnerable Plaque

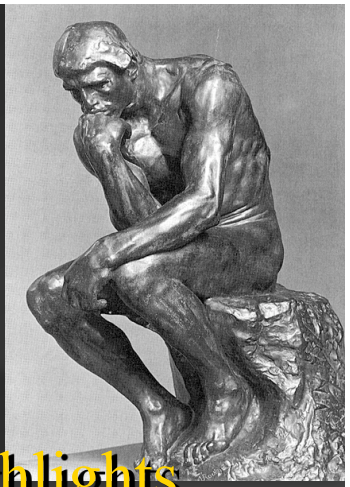


Korosoglou G. et al.: *J Am Coll Cardiol*. 2008 Aug 5;52(6):483-91.

Results: IRON Vessel Wall Enhancement (NER) vs. % Macrophage Area Watanabe Rabbits



Time to Reflect…



- What have we learned?
  - IRON MRI & superparamagnetic nanoparticles highlights areas of macrophage rich plaques.
  - Magnitude of enhancement is related to the amount of macrophages in Watanabe rabbits.
- What is needed to take this to the next level?
  - Translate to human setting!
- What would happen in the case of ultimate success?
  - Plaques with a high likelihood for rupture can be identified.

Team CIBM/CHUV

- Gabriele Bonanno
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- Andrew Coristine
- Helene Feliciano
- Maria Firsova
- Dr. Eleonora Fornari
- Dr. Ruud van Heeswijk

Siemens collaboration

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- Dr. Wolfgang Rehwald
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- Dr. Didier Locca
- Prof. Jürg Schwitter
- Prof. Pierre Vogt

EPFL collaboration

- Dr. Yves Wiaux
- Gilles Puy

NIH collaboration

- Dr. Michael Hansen

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- FBM

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Thank You!

Thank you!

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  - S. Kelle, MD
  - G. Korosoglou, MD
  - T. Lijun, MD
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  - M. Schaer, PhD
  - S. Shah, MS
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  - J. Yu, PhD
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  - D. Maintz, Muenster
  - W. Manning, MD, Harvard
  - D. Sodickson, PhD, MD, NYU
  - E. Spuentrup, MD, Aachen
  - Sites multicenter trial
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  - A. Arepally, MD
  - T. Balducci, MD
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