

– Ultrasound motion imaging –

In vivo validation

preamble





by

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Disclaimer: The views expressed in this course are those of the author and do not necessarily reflect the multiple positions of the ultrasound community. The examples may contain errors and can carry an implied judgement due to author's preference for one side of an issue over another.
Be critical and take a step back while reading this document!

what is a good gold standard?

- In scientific practice, a new method must be compared with an alternative that is considered to be the current standard (a "***gold standard***") in the field

- **Gold standard** is a historical term borrowed from economists. It represented a monetary standard, under which the unit of currency was defined by a stated quantity of gold. This made it possible to compare different currencies for international trading. (source: BMJ. 2005;330:1121)

- In science, the gold standard is not the perfect test but merely the best available test (source: BMJ. 1992;305:187)

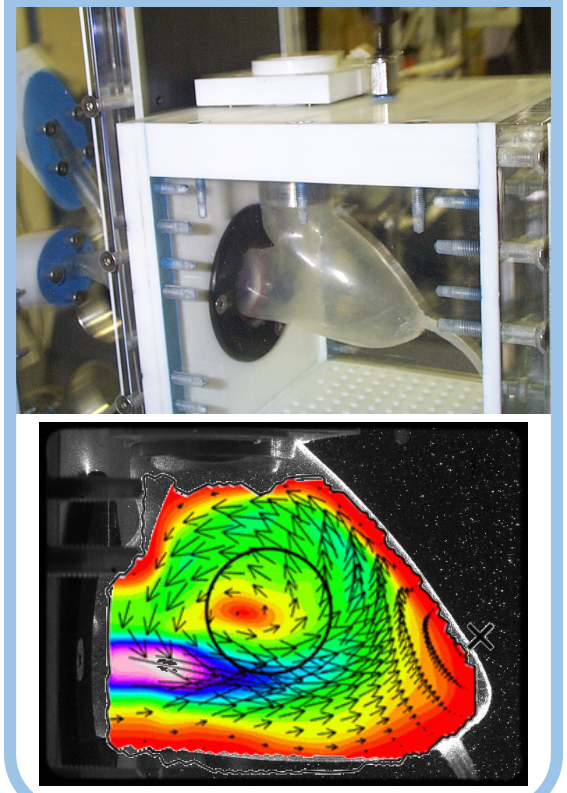
But often, the gold standard is impossible to perform on a living person!
(biopsy, invasiveness, ionizing radiation…)

An ideal protocol should contain the three "*in*" steps

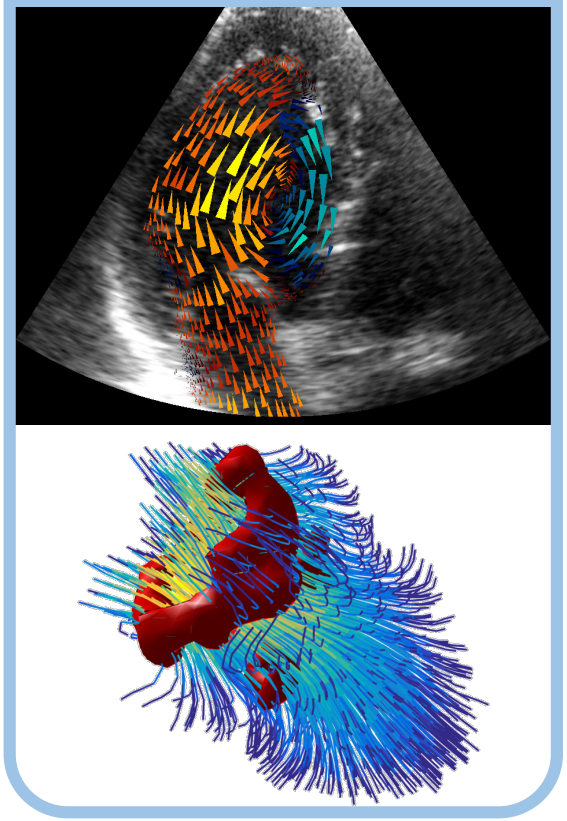
in silico



in vitro



in vivo



- **understand**
- **develop**
- **verify**

if it works →

- **optimize**
- **double-check**
- **validate**

if it works →

- **fine-tune**
- **confirm**
- **publish**

if it works → **PUBLISH**

otherwise ↑ (back to understand/develop/verify)

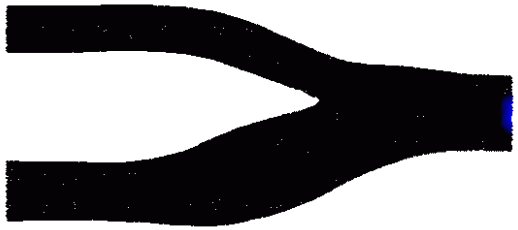
otherwise ↑ (back to optimize/double-check/validate)

otherwise ↑ (back to fine-tune/confirm/publish)

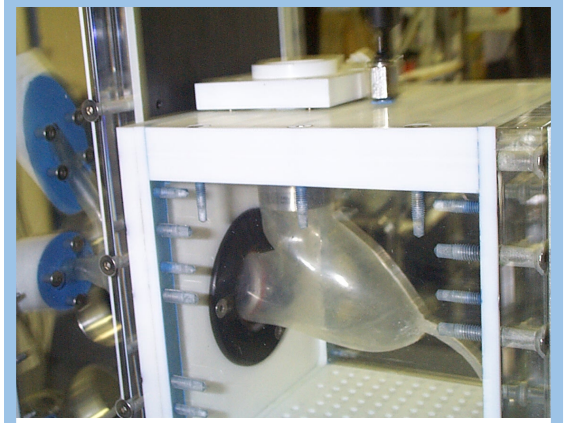
a good protocol

An ideal protocol should contain the three "*in*" steps

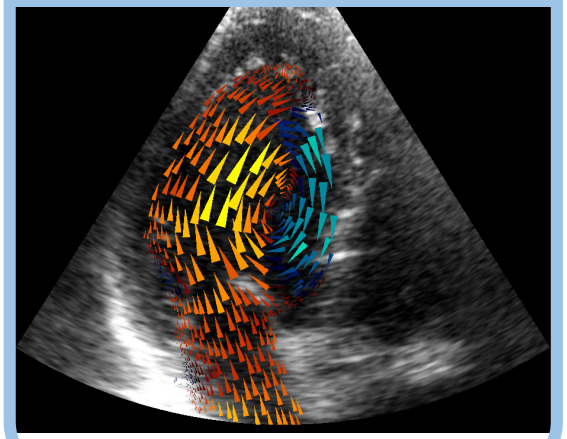
in silico



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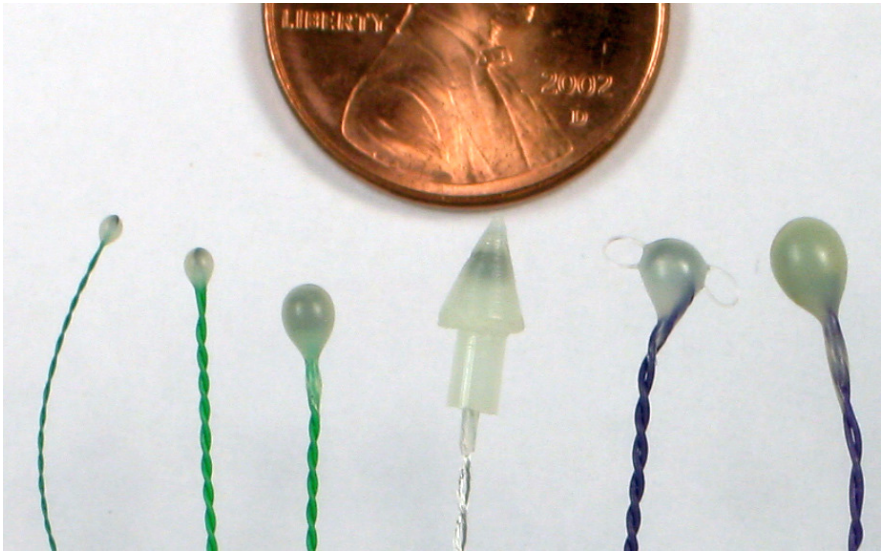
otherwise ↑ (from validate)

otherwise ↑ (from publish)

It's not that easy! One must consider skills, time, money, staff, facilities…

sonomicrometry

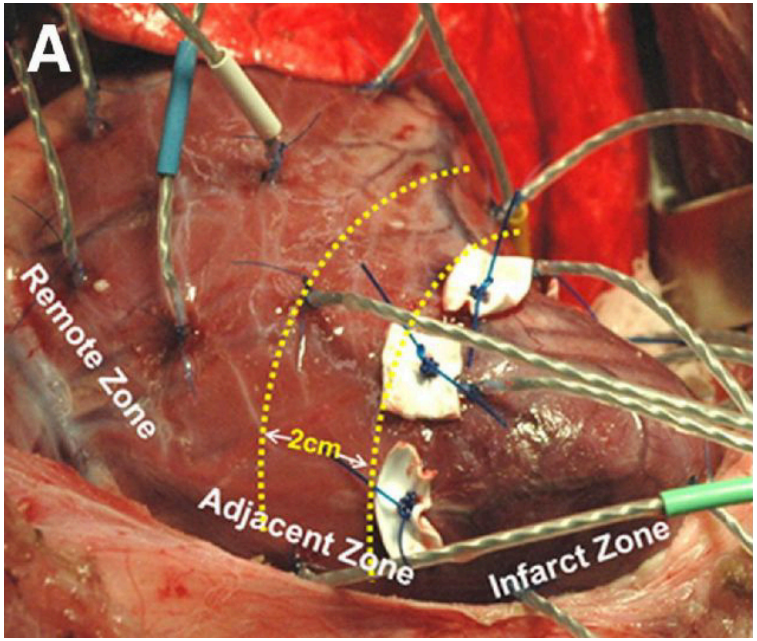
- **Sonomicrometry** measures distances between a number of piezoelectric crystals
- It is based on the times of flight of acoustic signals
- It can be applied in the study of cardiac volume/motion in research animals



https://en.wikipedia.org/wiki/Sonomicrometry

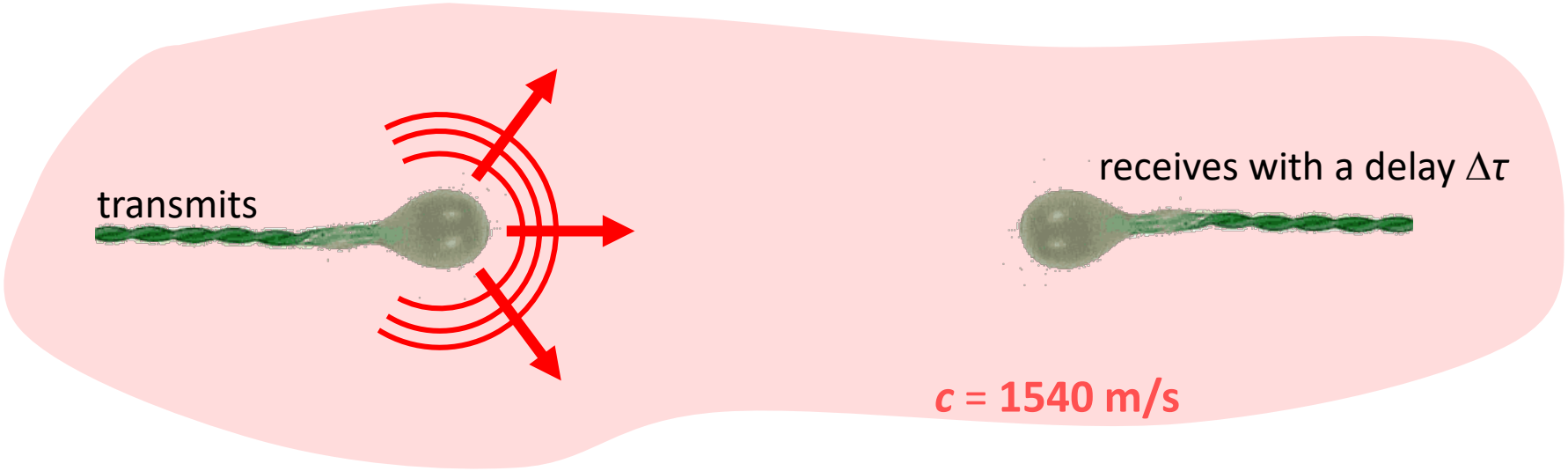
sonomicrometry (cont'd)

- Animal experiments
- Open-chest



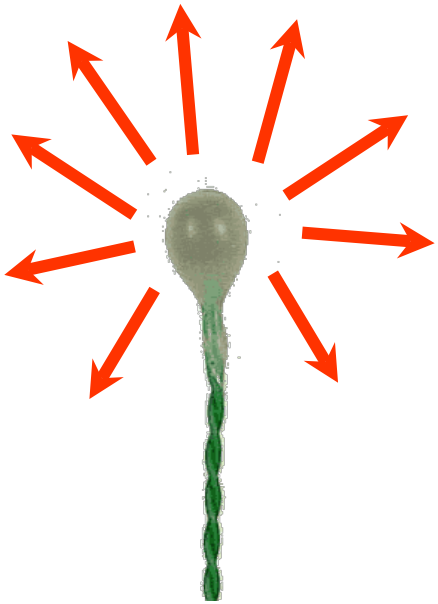
source: Wei *et al*. JACC: Cardiovascular Interventions. 2013;6(4):406-15.

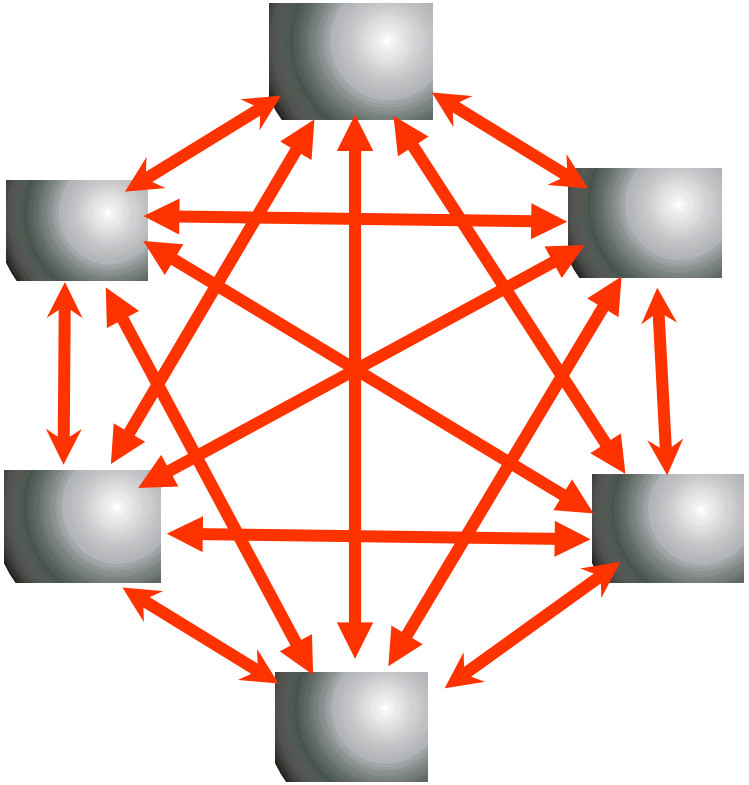
sonomicrometry: basics



$$\text{distance} = c\,\Delta\tau$$

sonomicrometry: basics (cont'd)



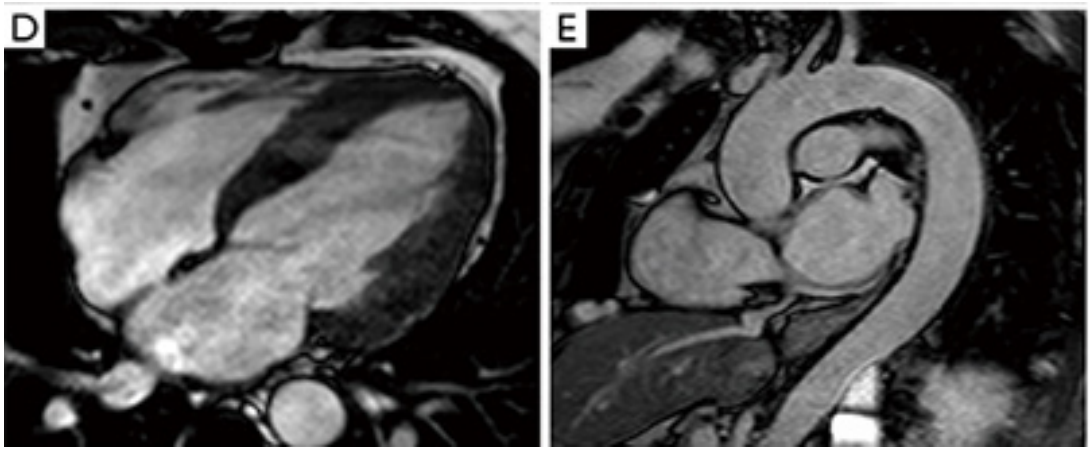


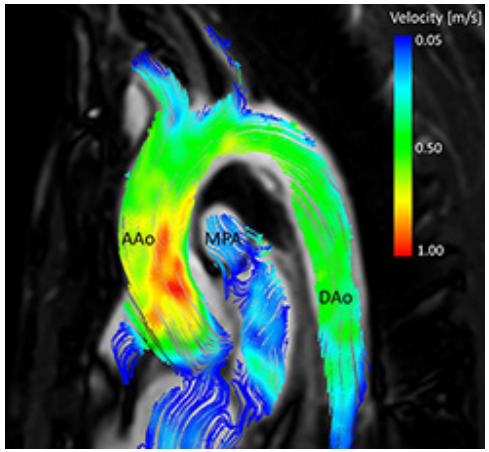
- **Sonomicrometry** returns distances between <u>each pair</u> of crystals
- instantaneous distances on a moving surface $\Rightarrow$ volumes, strains, strain rates

In medical imaging, magnetic resonance imaging (MRI) is often considered to be a gold standard

- non invasive
- non ionizing
- high-quality
- 3D + time
- flow and tissue



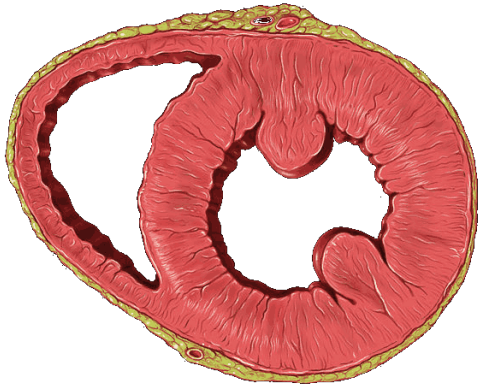


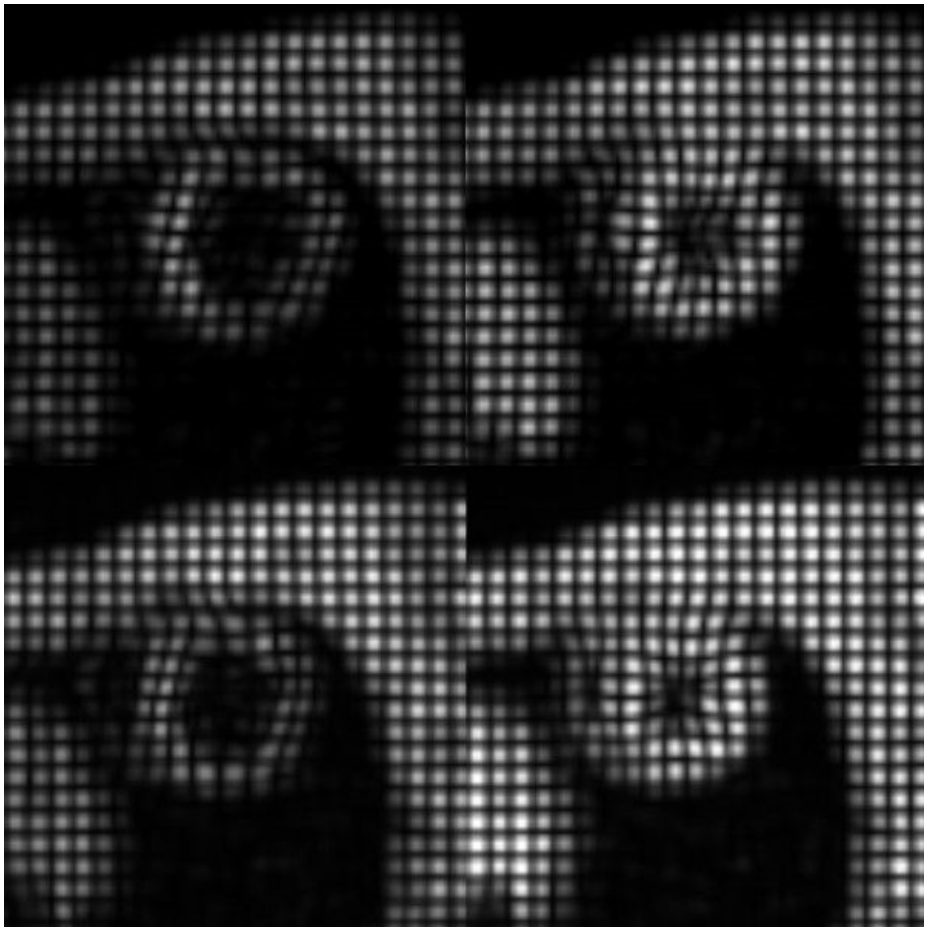


source: Al Musa *et al*. Quantitative imaging in medicine and surgery. 2016;6:259.

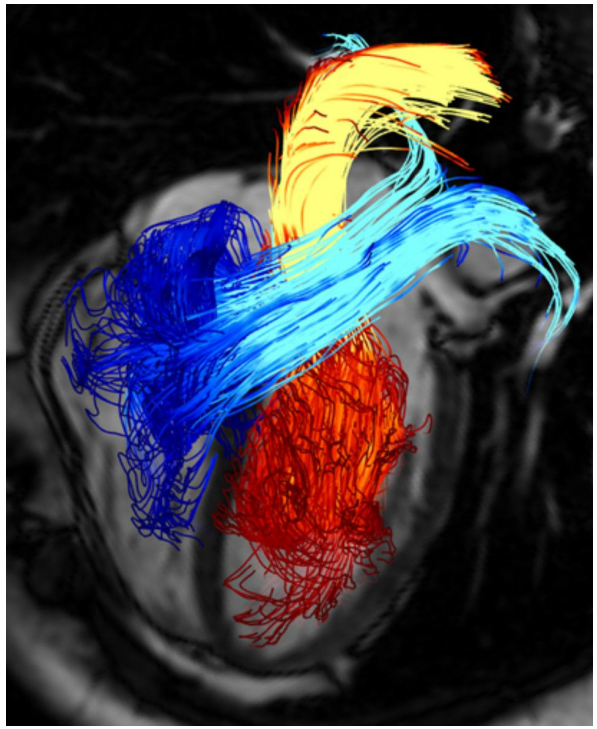
MRI tagging

With MRI tagging, the deformations are visible and (of course) measurable





4D velocity mapping by CMR



source: Markl, Kilner, Ebbers Journal of Cardiovascular Magnetic Resonance 2011;13:7.

In vivo cardio-vascular motion measurements using Magnetic Resonance Imaging

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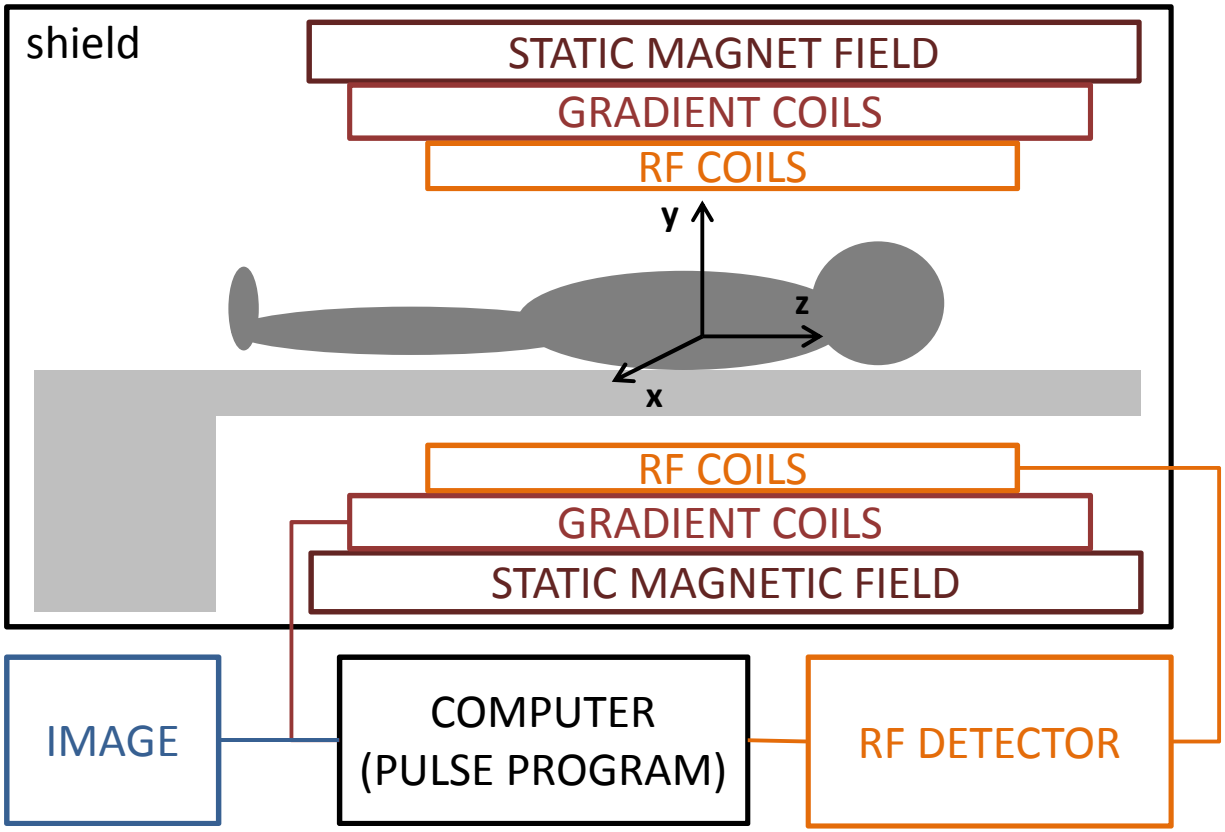
Outline

- MRI basics
  - Spin physics in the classical description
  - From spin to image
- Methods for motion measurement in MRI:
  - Magnitude based
    - Magnetization modulation: SPAMM, DANTE, CSPAMM, SENC
  - Phase based
    - DENSE, Phase Contrast-MRI

Components of an MRI system

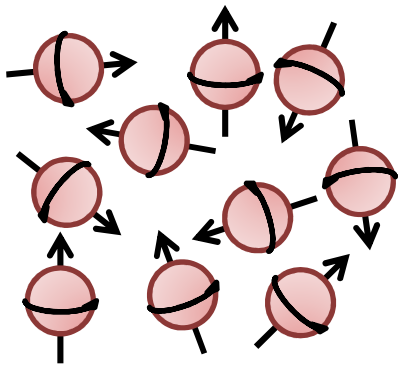


> 2 m in height
2 - 6 tons in weight
50k * > Earth's magnetic field
Clinical fields 1.5 & 3T

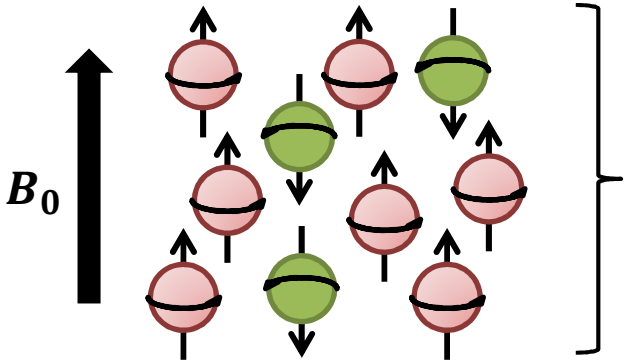


The proton –> a magnetic dipole

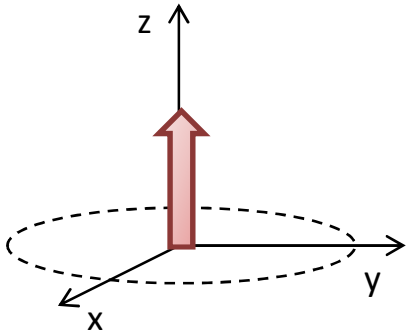
- MRI uses the magnetic properties of ^{1}H (but also ^{19}F, ^{23}Na, ^{31}P) to produce images. The human body is 70% H_2O
- The ^{1}H nucleus has one proton, a charged particle that is spinning around it's axis. This spin produces a magnetic moment (dipole).



No applied field



Applied field (B_0)



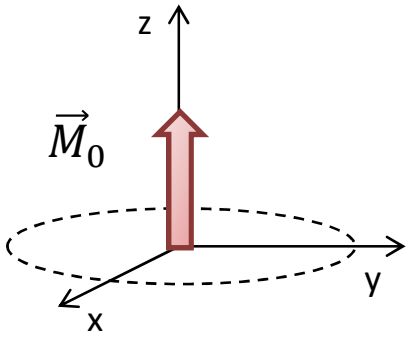
Net magnetization ($\vec{M}_0$)

Nuclear Magnetic Resonance (NMR)

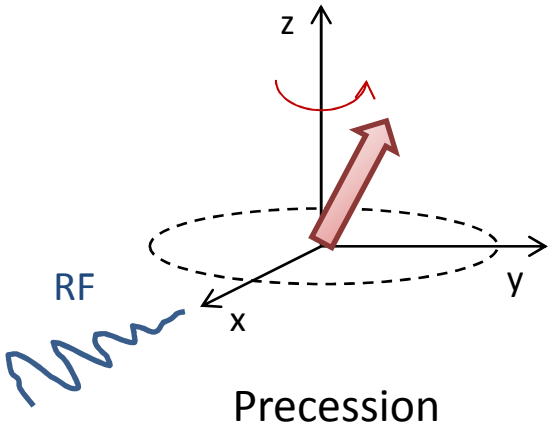
- The NMR phenomenon:
  - The precession (oscillating response) of $\vec{M}_0$ when it receives energy from an RF pulse at the Larmor frequency (f_0)



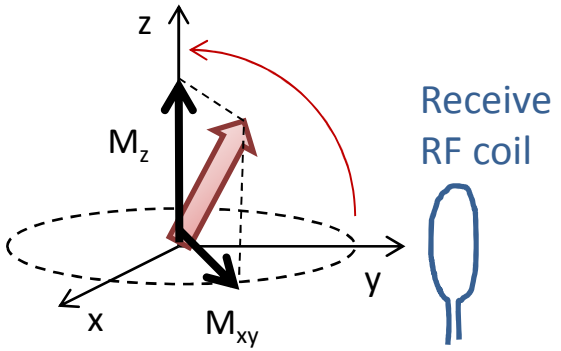
$f_0 = \gamma B_0$, γ – *gyromagnetic ratio,* *42.58 MHz/T for protons*



Equilibrium



Precession

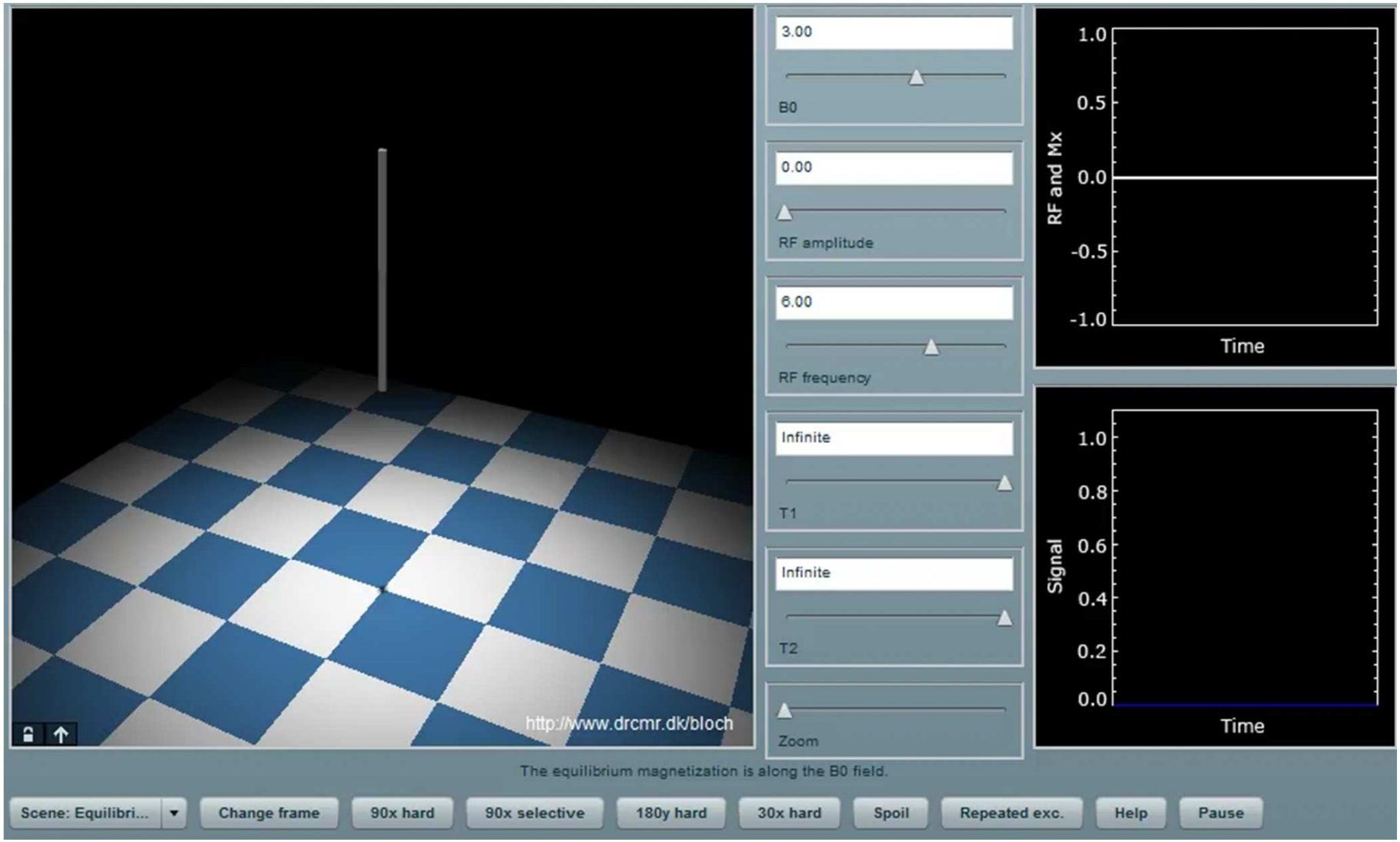


Relaxation:

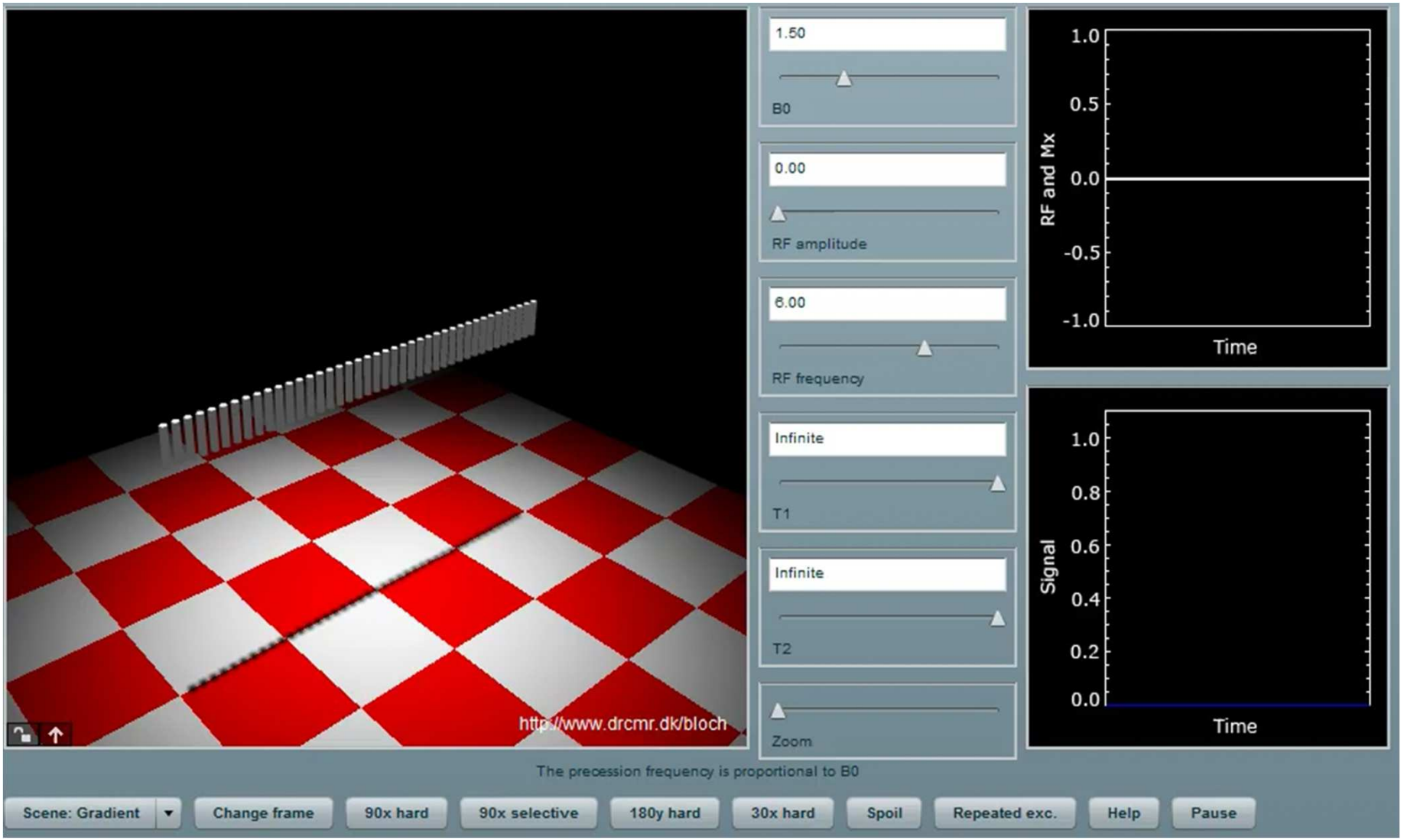
T1 – longitudinal: $M_z = M_0(1 - e^{-t/T_1})$

T2 – transverse: $M_{xy} = M_0 e^{-t/T_2}$

[Bloch F., Phys Rev 1946]

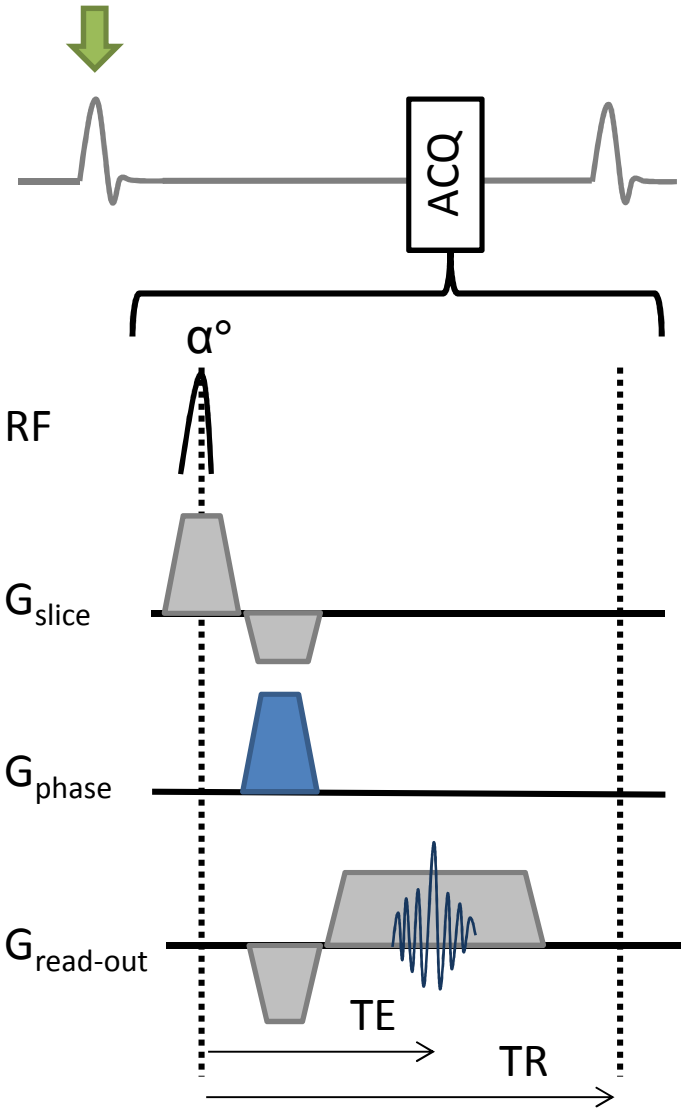


[Dr. LG Hanson, DTU http://www.drcmr.dk/BlochSimulator]

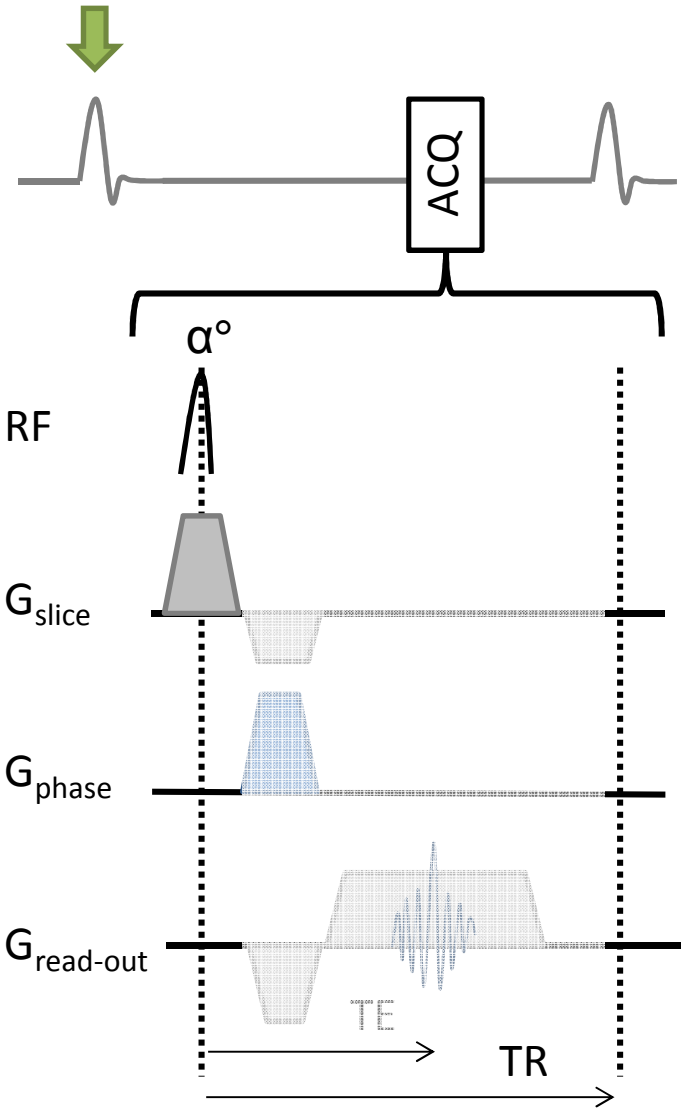


[Dr. LG Hanson, DTU http://www.drcmr.dk/BlochSimulator]

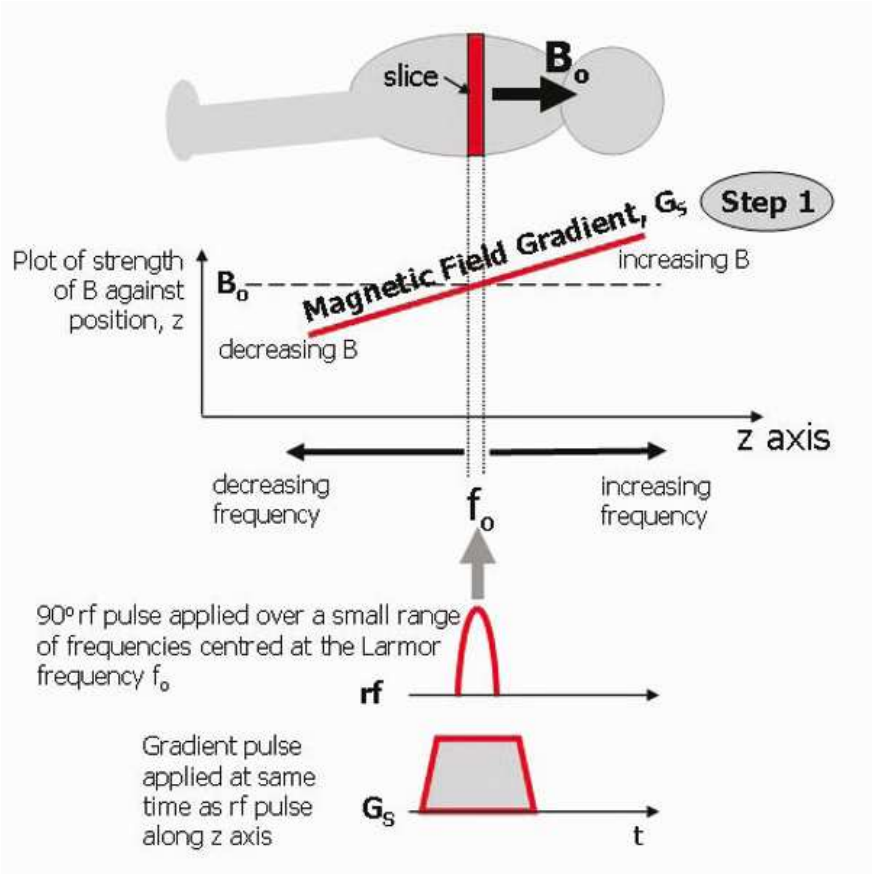
Timeline of image generation



Timeline of image generation

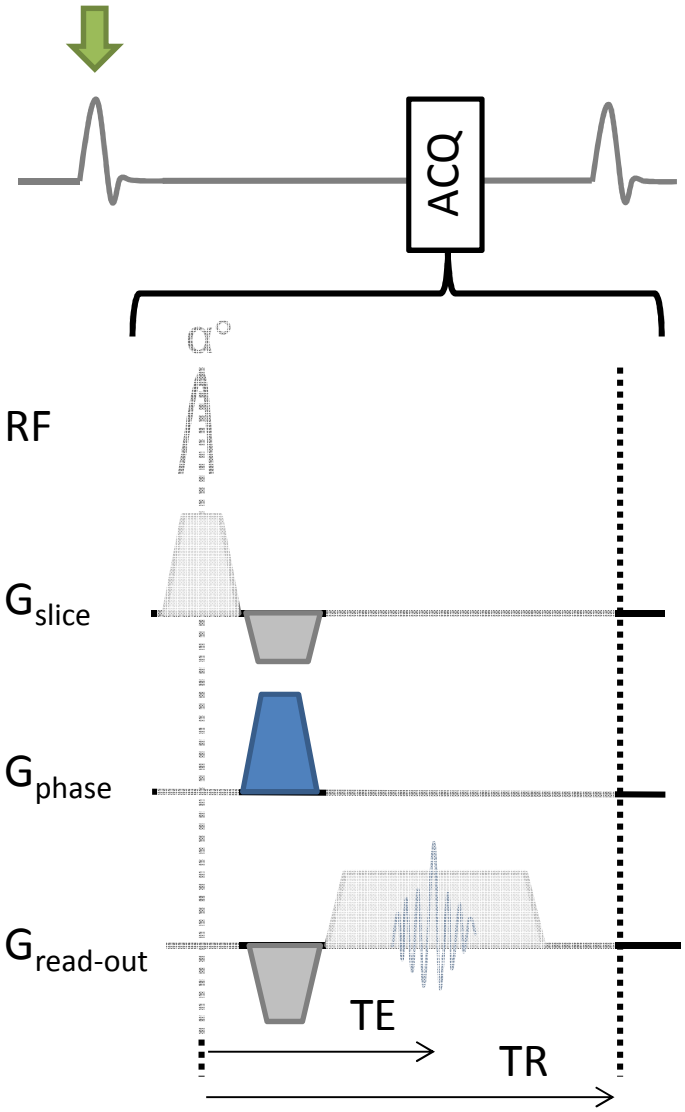


Step 1 – Slice selection

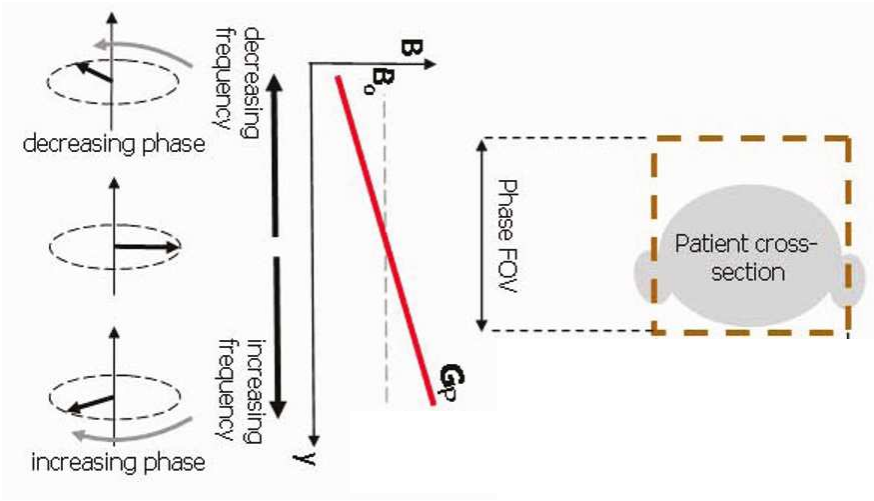


[Ridgway JP., JCMR 2010]

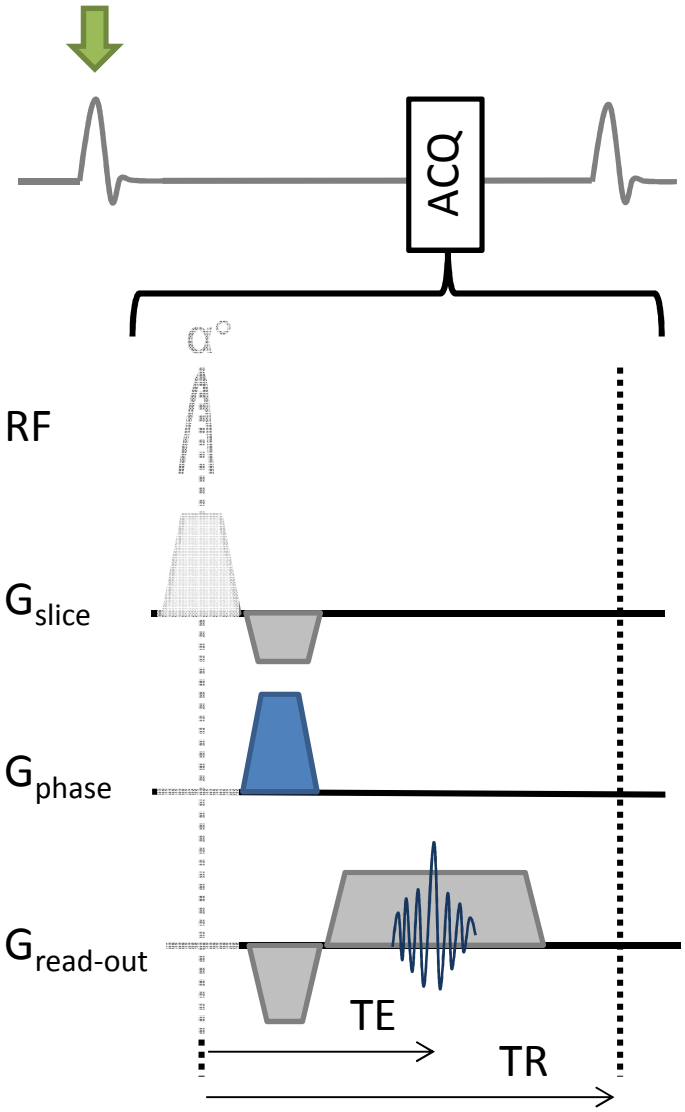
Timeline of image generation



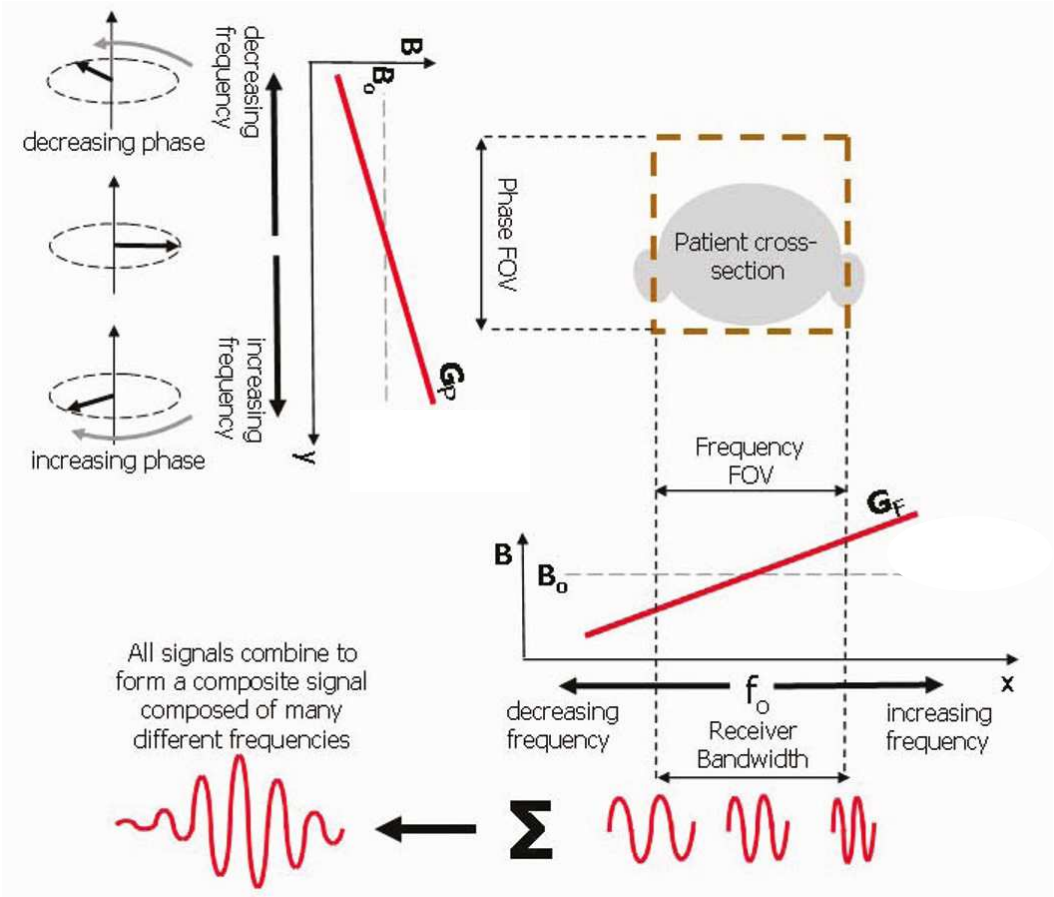
Step 2 – Phase encoding



Timeline of image generation

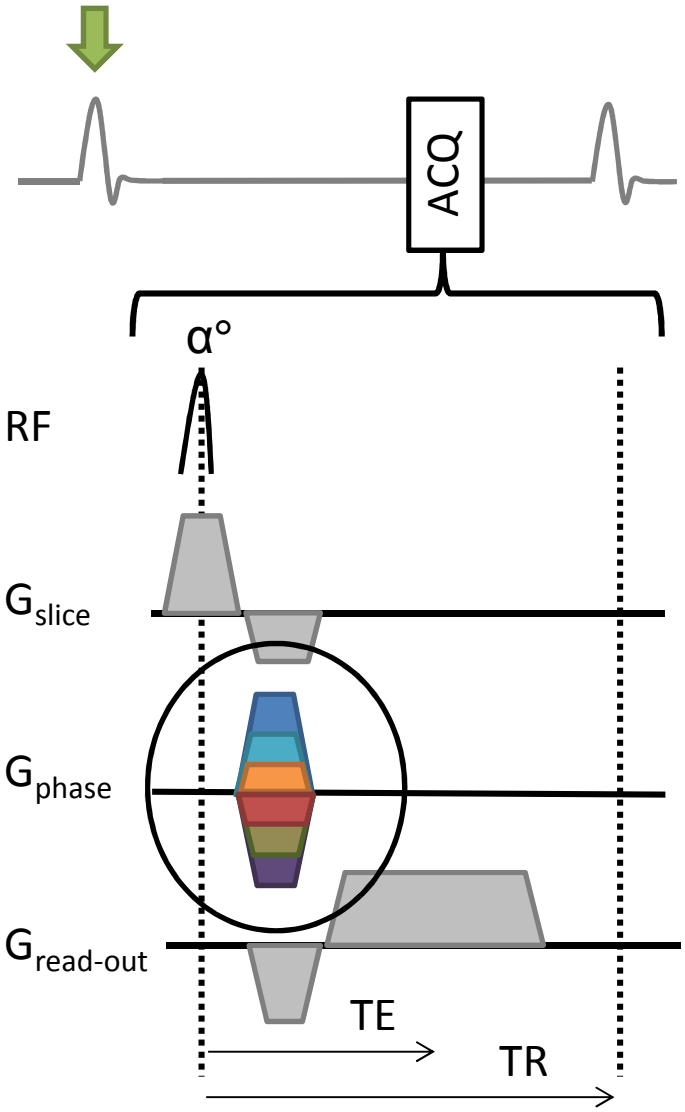


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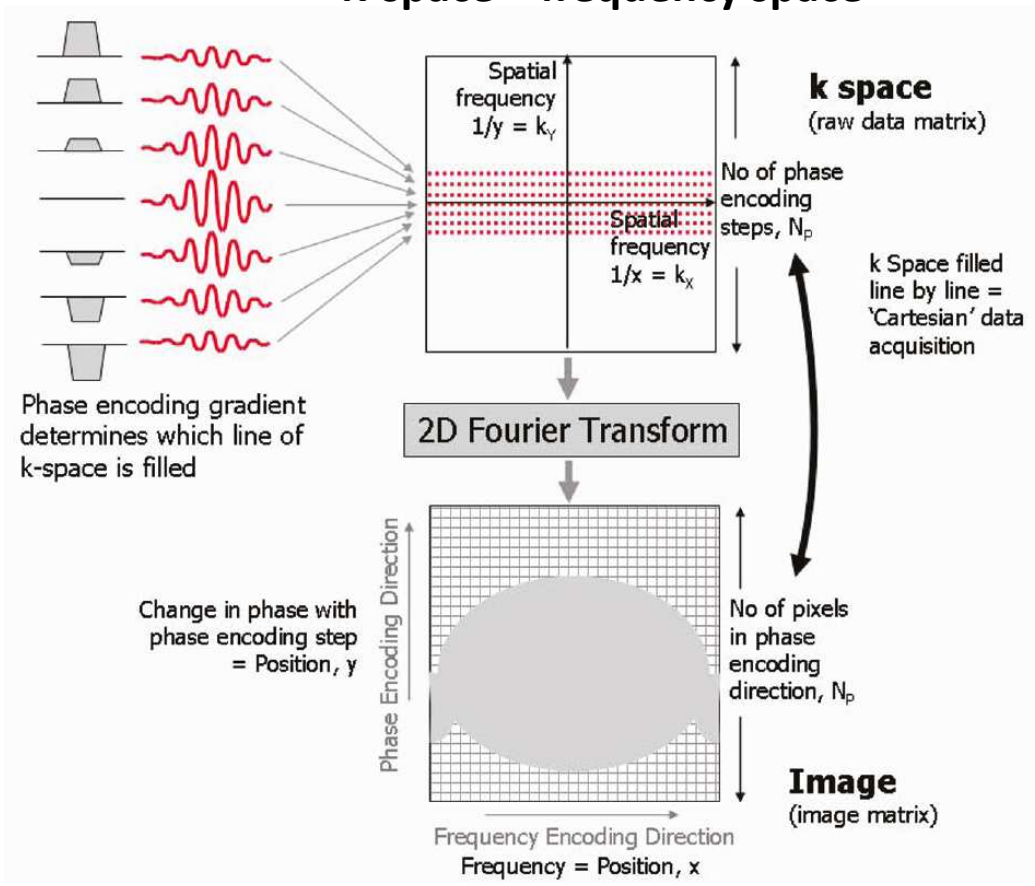


Step 3 – Frequency encoding

Timeline of image generation



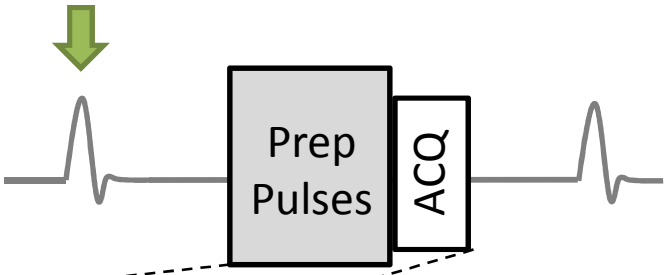
K-space = frequency space

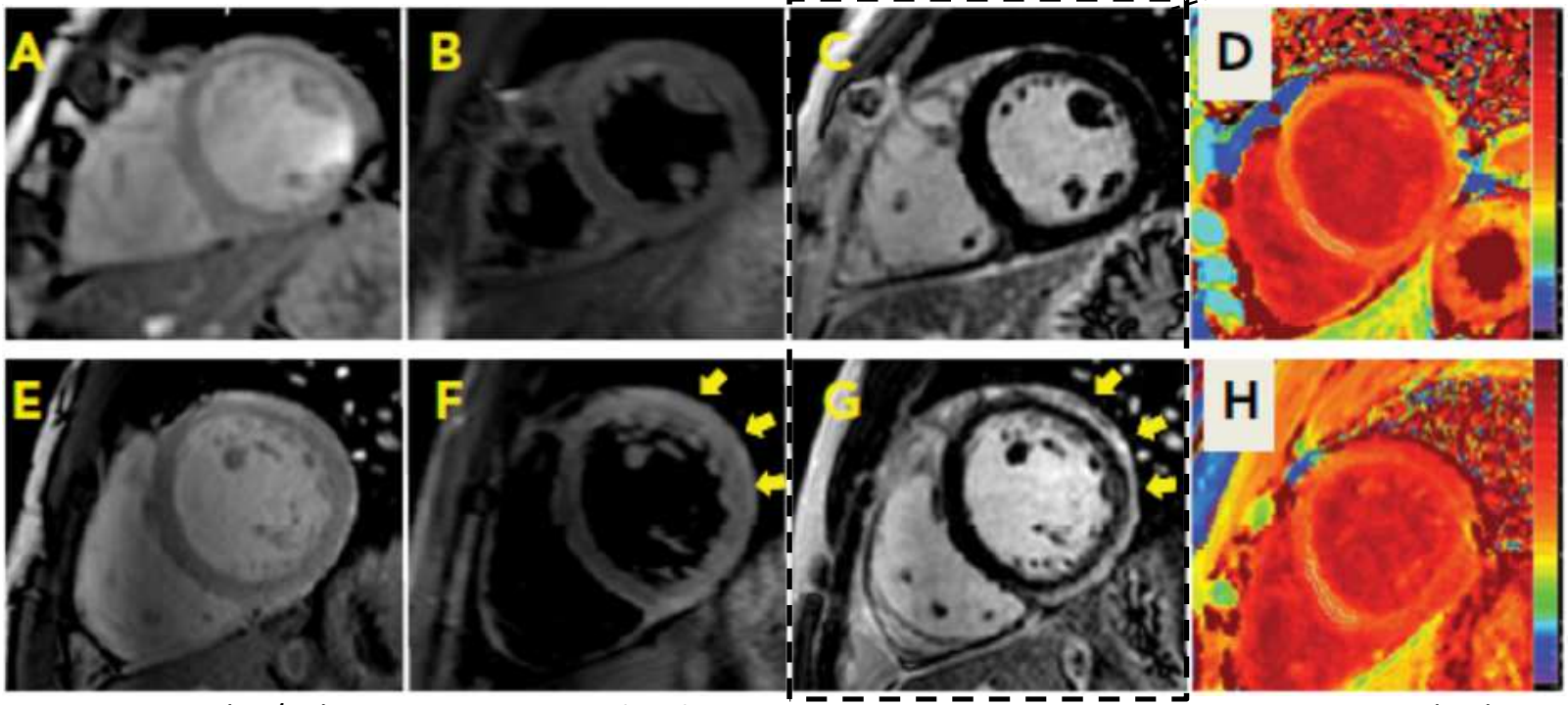


[Ridgway JP., JCMR 2010]

Understanding image contrast

- Optimize image contrast by the
  - imaging parameters (TR, TE, α),
  - specificity of the imaging sequence,
  - magnetization preparation: FatSat, IR,…

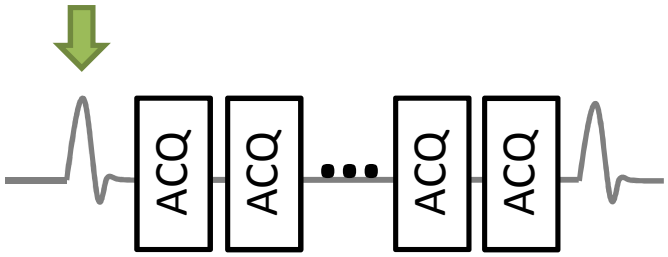


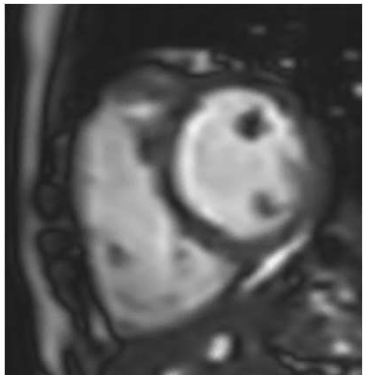


Cine SSFP (T2/T1) | T2 weighted | IR T1 weighted | T1 mapping (ms)

[Hinojar R. et al, *European Cardiology Review* 2016]

Clinical standard for the heart function evaluation

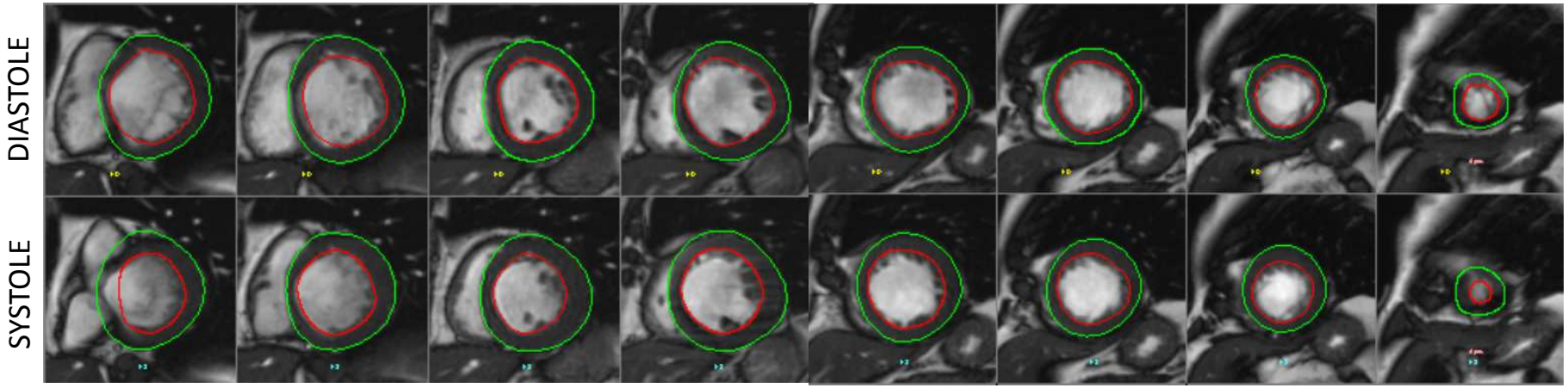




Global measures:
stroke volume (SV),
ejection fraction (EF),
myocardial thickness,...

SV = EDV – ESV
*EF(%) = SV/EDV * 100*

Spatial resolution: 1-2mm in-plane and ~ 8mm slice
Temporal resolution: ~ 20-40 phases / cardiac cycle



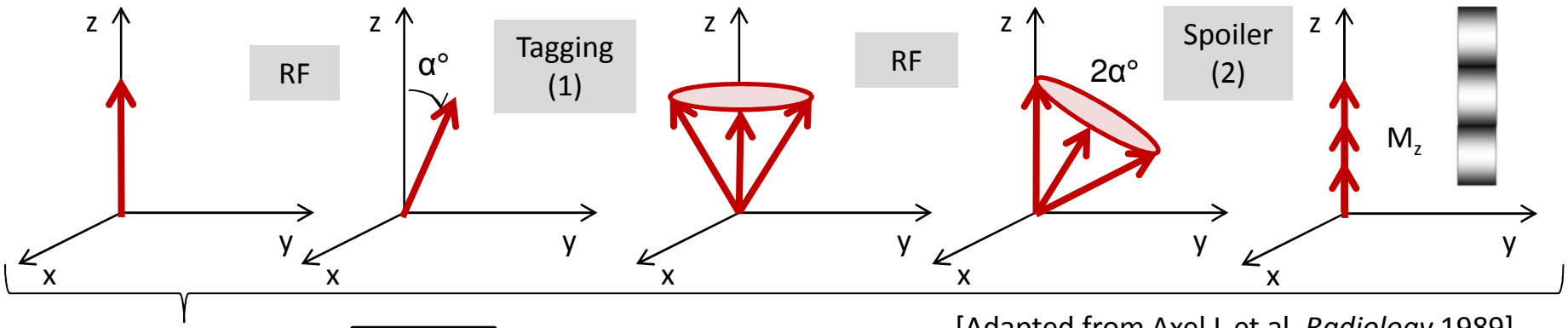
- Global measures are insensitive to alterations of the regional performance
- Lack of intrinsic myocardial markers -> intramural motion components cannot be evaluated correctly

Myocardial Tagging by MRI

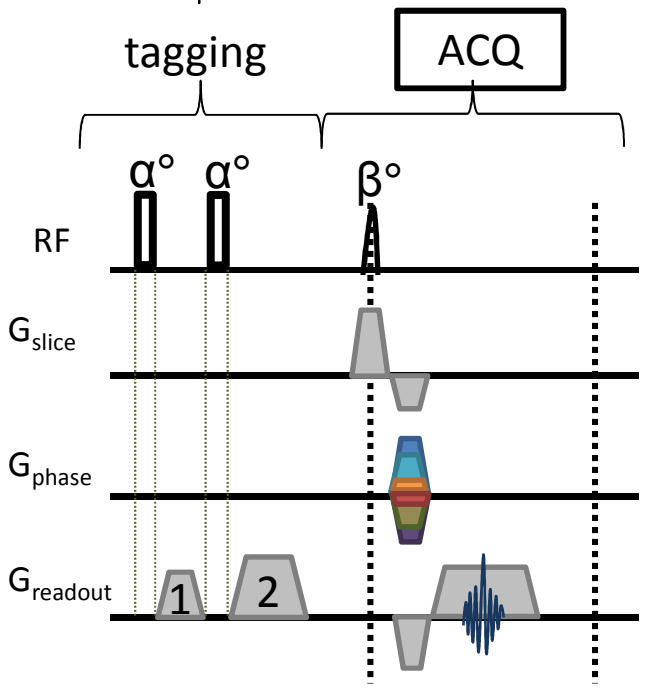
- Invented in 1988 as a way to create markers in the myocardium by magnetization modulation [1]
- Subsequent developments and improvements resulted in a series of methods:
  - Stage 1 - basic techniques: **SPAMM[2], DANTE[3], CSPAMM[4]**
    - Visible pattern of magnetization saturation (parallel lines, grid pattern, radial stripes) and visual inspection of contractility
    - Cumbersome post-processing (complicated algorithms + long analysis times)
  - Stage 2 - advanced techniques: **HARP[5], DENSE[6], SENC[7]**
    - K-space based methods, no visible pattern in image magnitude
    - Simple and fast post-processing

[1][Zerhouni EA et al, *Radiology* 1988], [2][Axel L et al, *Radiology* 1989], [3][Mosher TJ et al, *Magn Reson Med* 1990], [4][Fischer SE et al, *Magn Reson Med* 1993], [5][Osman NF et al, *Magn Reson Med* 1999], [6][Aletras AH et al, *J Magn Reson* 1999], [7][Osman NF et al, *Magn Reson Med* 2001]

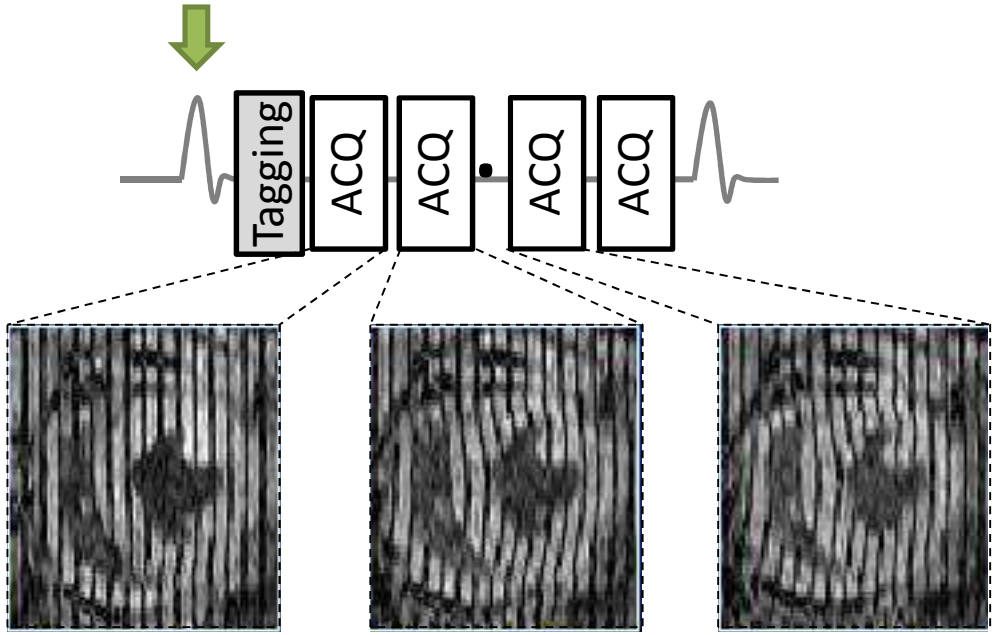
SPAtial Modulation of Magnetization (SPAMM)



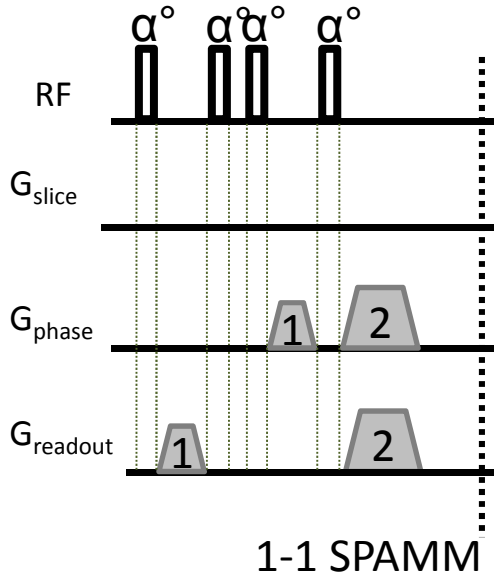
[Adapted from Axel L et al, *Radiology* 1989]



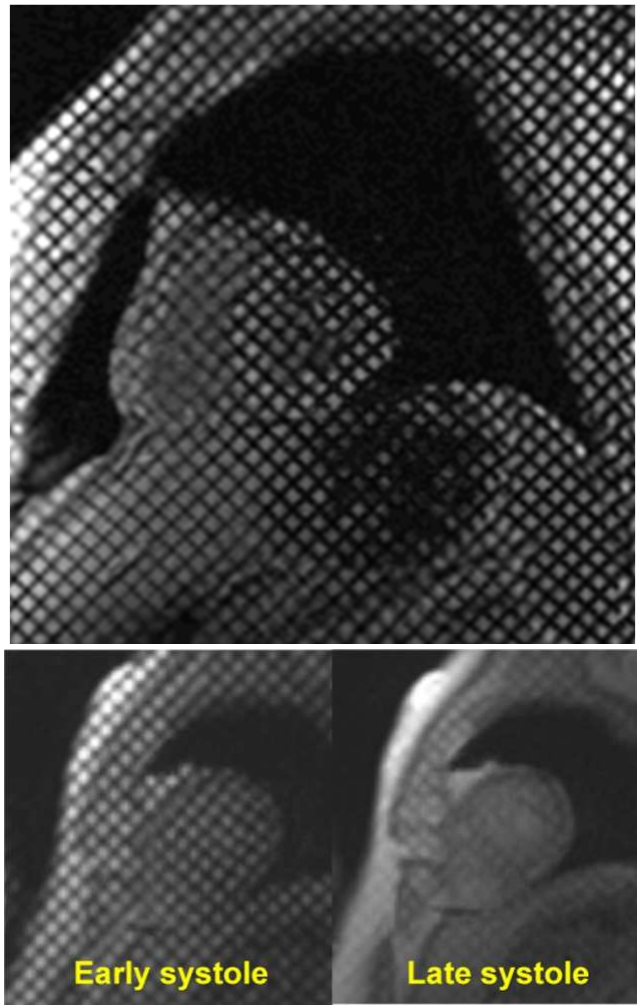
1-1 SPAMM Pulse sequence



SPAtial Modulation of Magnetization (SPAMM)

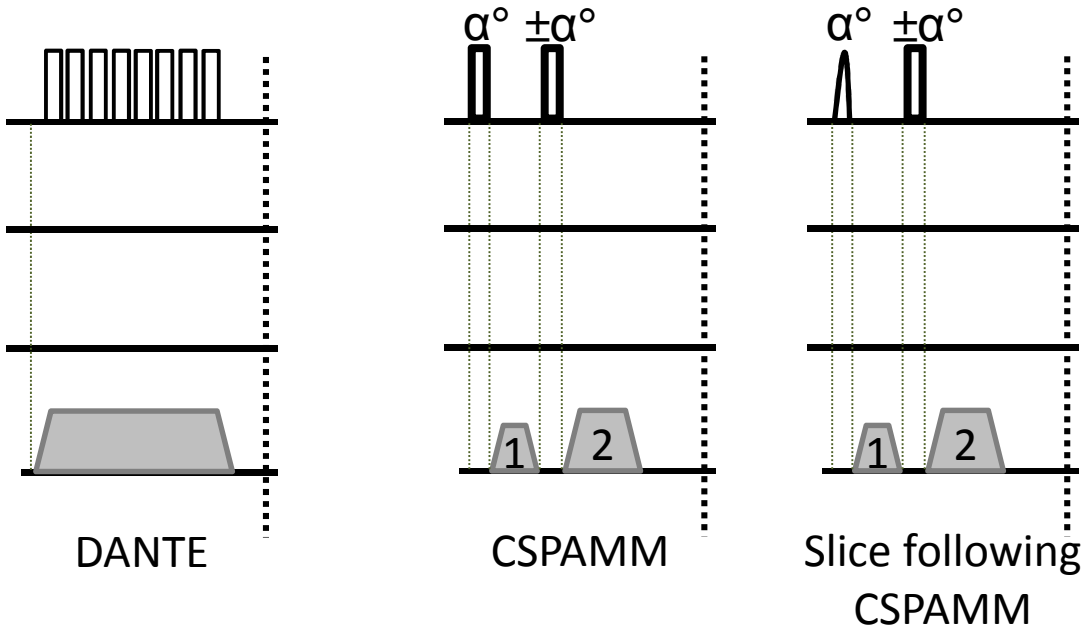


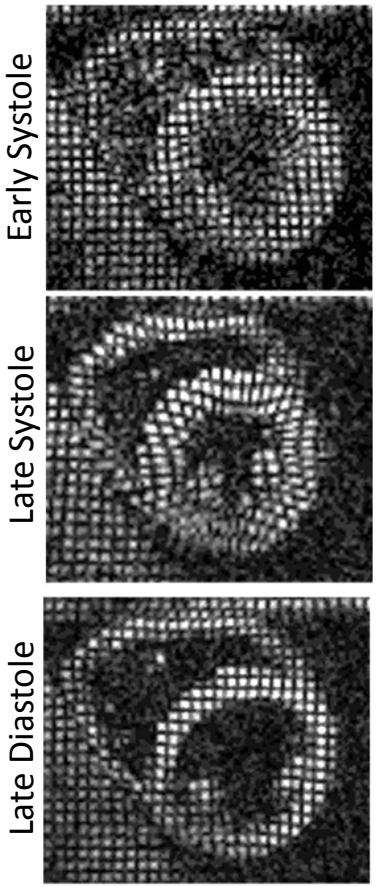




SPAtial Modulation of Magnetization (SPAMM)

- Improvements on the 1-1 SPAMM:
  - High order SPAMM: 1-2-1, 1-3-3-1 -> sharper tag lines
  - DANTE- high density of thin tags
  - CSPAMM -> addressed SNR and the fading of the tags
    - Doubles the scan time
  - Slice following CSPAMM
    - Lower SNR than CSPAMM

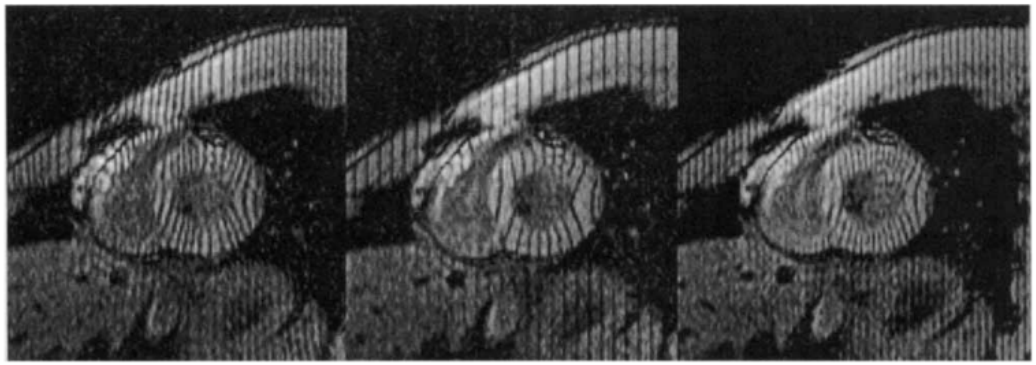




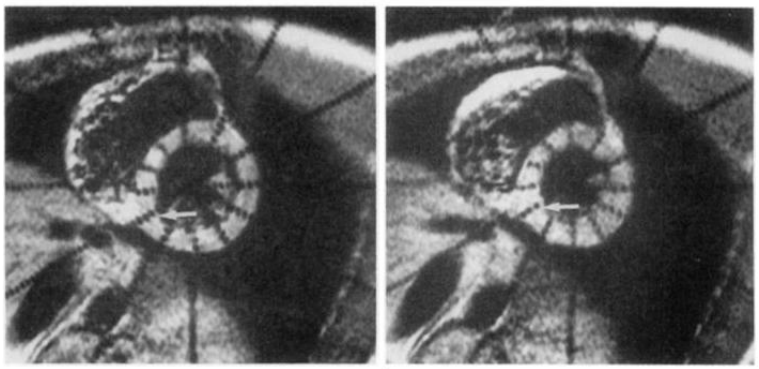
CSPAMM with spiral readout: temporal resol 35 msec, 1.5x1.5 mm pixel and 4 mm tag spacing [Ryf S et al, *MRM 2004*]

SPAtial Modulation of Magnetization (SPAMM)

- Improvements on the 1-1 SPAMM:
  - High order SPAMM: 1-2-1, 1-3-3-1 -> sharper tag lines
  - CSPAMM -> addressed SNR and the fading of the tags
    - Doubles the scan time
  - Slice following CSPAMM
  - Localized and Variable density SPAMM -> more sensitive motion estimates
    - Requires customization of the pattern to the expected motion
  - Radial tagging



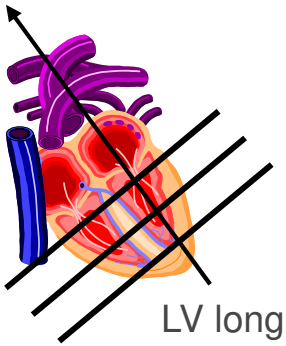
[McVeigh E et al, *Magn Reson Med* 1998]



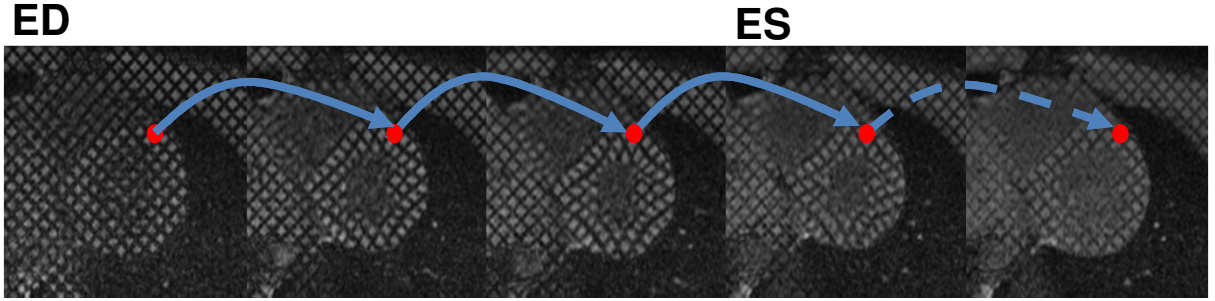
Systole Diastole

[Bolster B et al, *Radiology* 1990]

Motion quantification in MR tagging



LV long axis



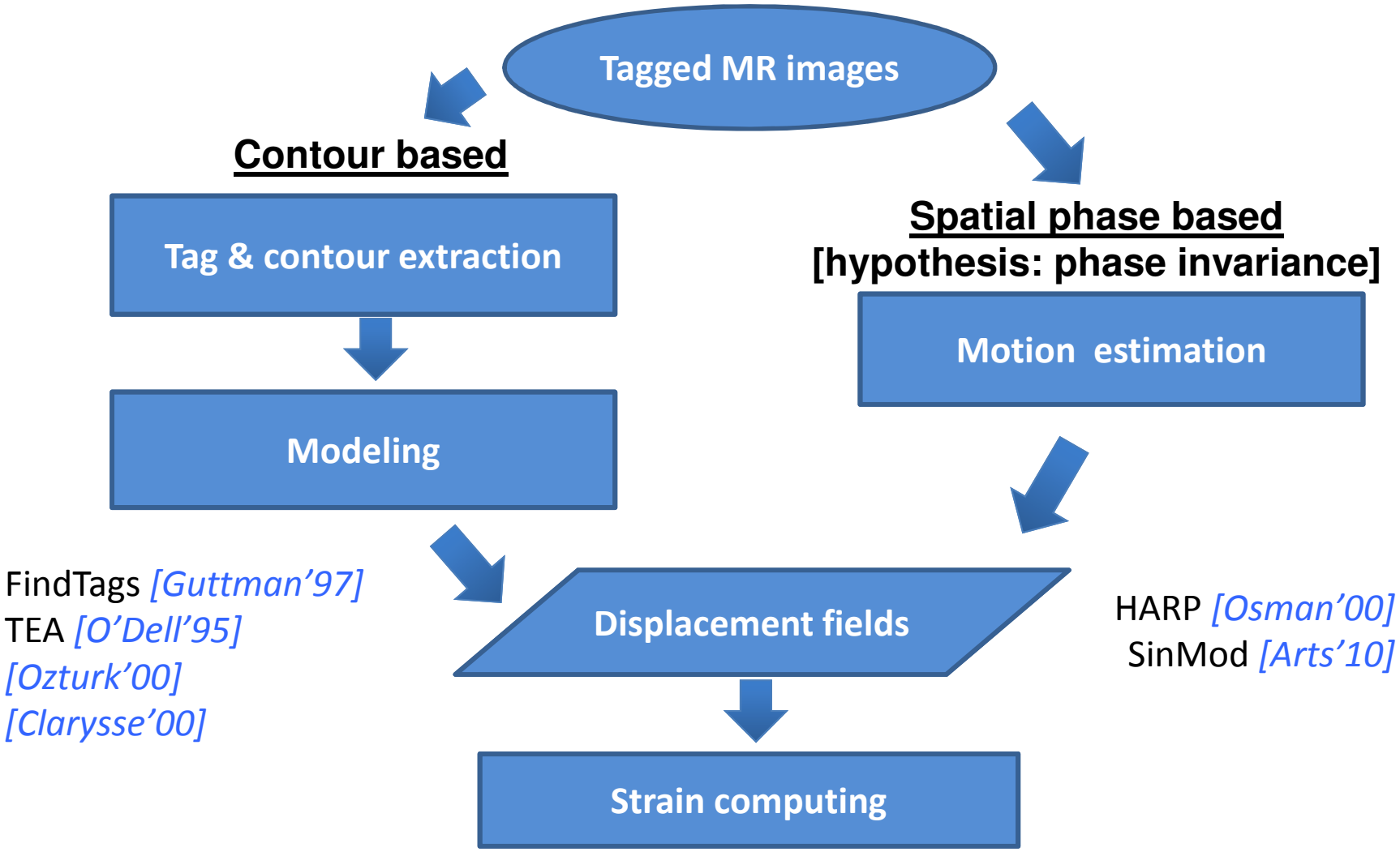
➔ **A material point correspondence problem**

Time

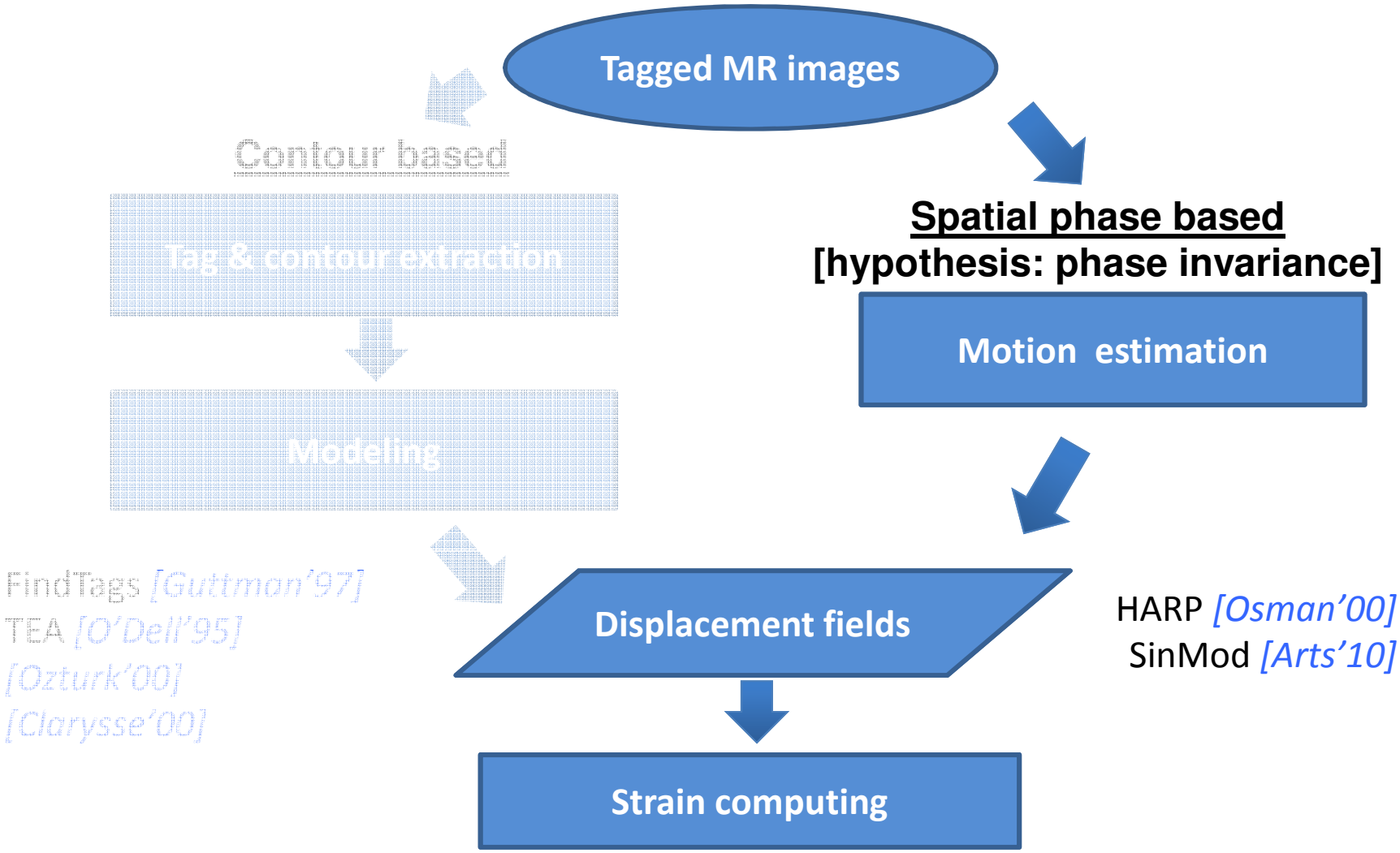
Method	Characteristics	Advantages	Disadvantages
Active contour	Uses spline curves that are fitted to the tag lines using multiple constraints.	Intuitive approach; parametric continuity; local control of the curve shape.	Long processing time; sensitive to weights of different constraint forces.
Optical flow	Tracks tag lines intersections based on tagging contrast.	Possibility for automatic processing; reduced processing time.	Sensitive to image quality, especially tagging contrast.
Template matching	Cross-correlates a pre-defined tagging pattern with the resulting images.	Reduced processing time.	Pre-defined assumptions must be met.
Sinusoidal analysis	Data are analyzed into different frequency components.	Decreased sensitivity to noise; high accuracy.	Complicated data analysis.
Volumetric modeling	Analyzes a stack of parallel tagged images.	3-D tagging analysis; more automatic processing.	Long processing time.
Finite-element modeling	Creates model tags, which define the tag lines in the images.	3-D tagging analysis; reduced processing time.	Measurements are not directly related to clinical understanding.
Statistical modeling	Uses statistical methods for estimating tag lines deformation.	3-D capability; more intuitive and understandable parameters.	Predefined assumptions; complicated processing.
3-D active contour modeling	Uses 3-D spline curves that are fitted to tag lines from a set of parallel images.	3-D capability; high resolution; parametric continuity.	Long processing time.

[Ibrahim et al, *JCMR* 2011]

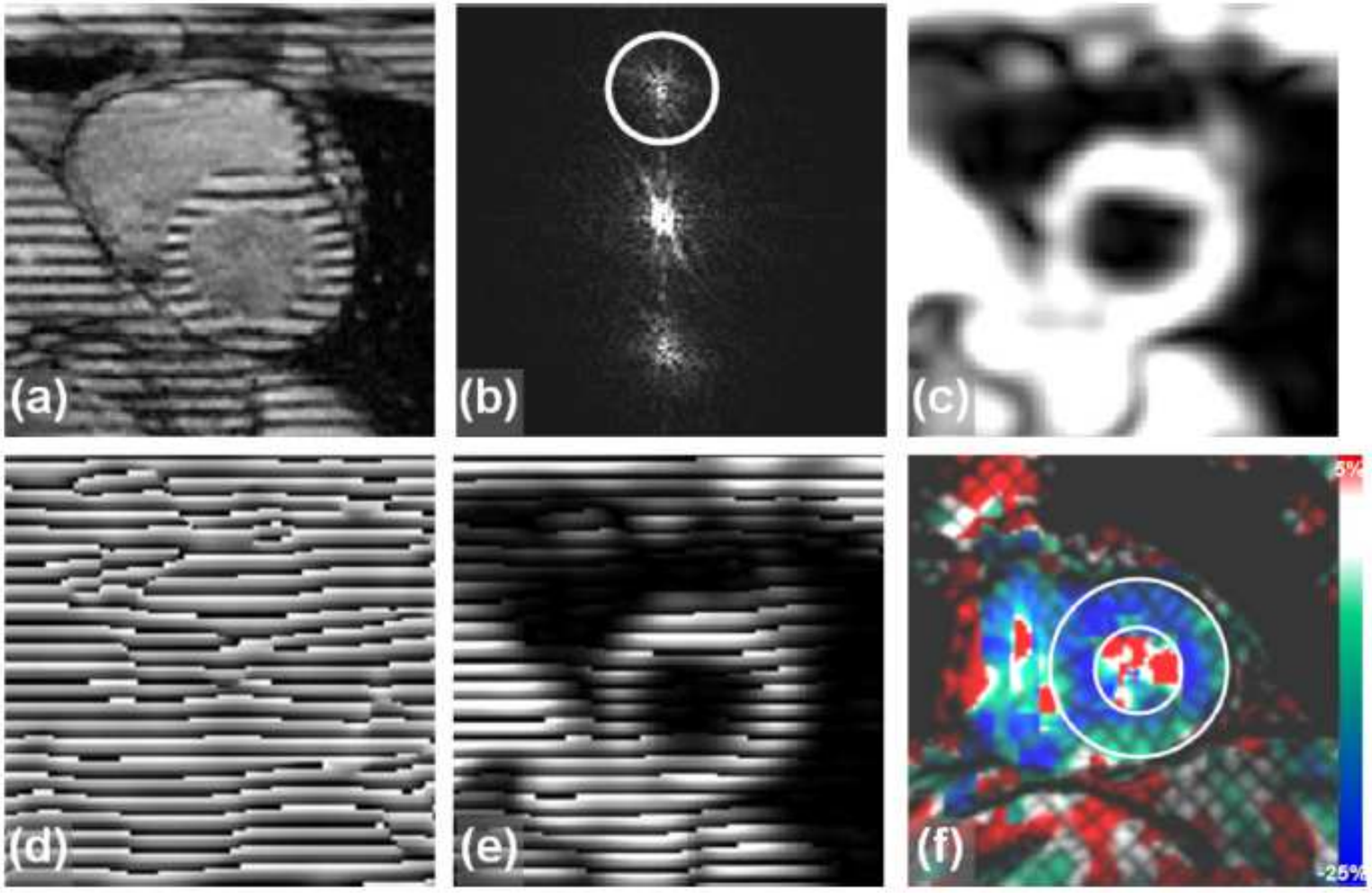
Post-processing for basic MR Tagging



Post-processing for basic MR Tagging

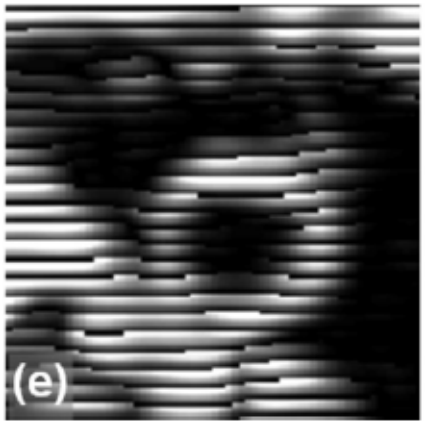


HARmonic Phase (HARP)

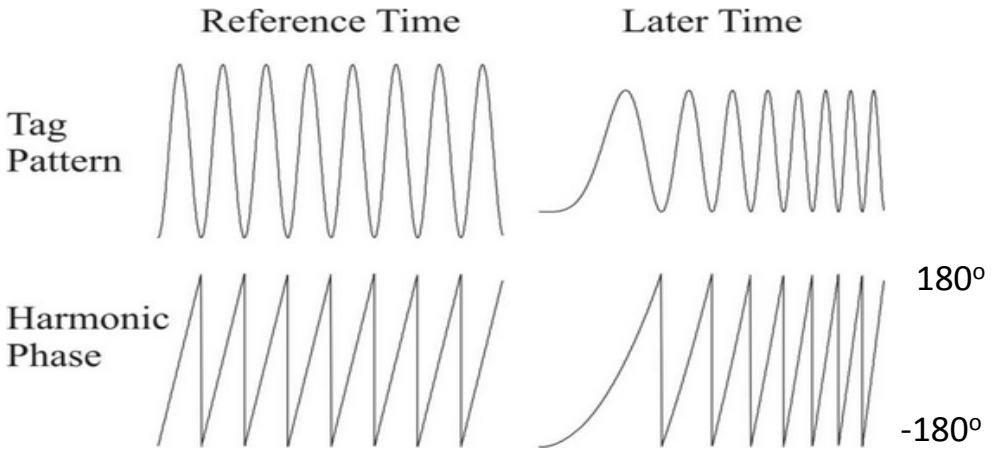


[Osman et al, *IEEE Trans Med Imaging* 2000; Osman et al, *Phys Med Biol* 2000]

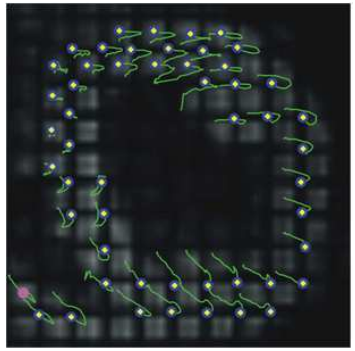
HARmonic Phase (HARP)



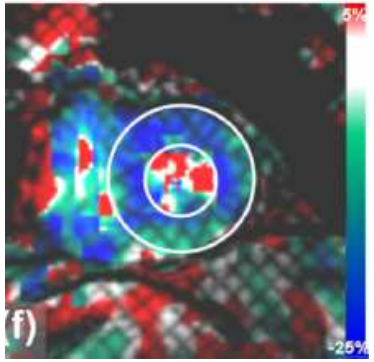
HARP Phase image



Optical flow based motion tracking

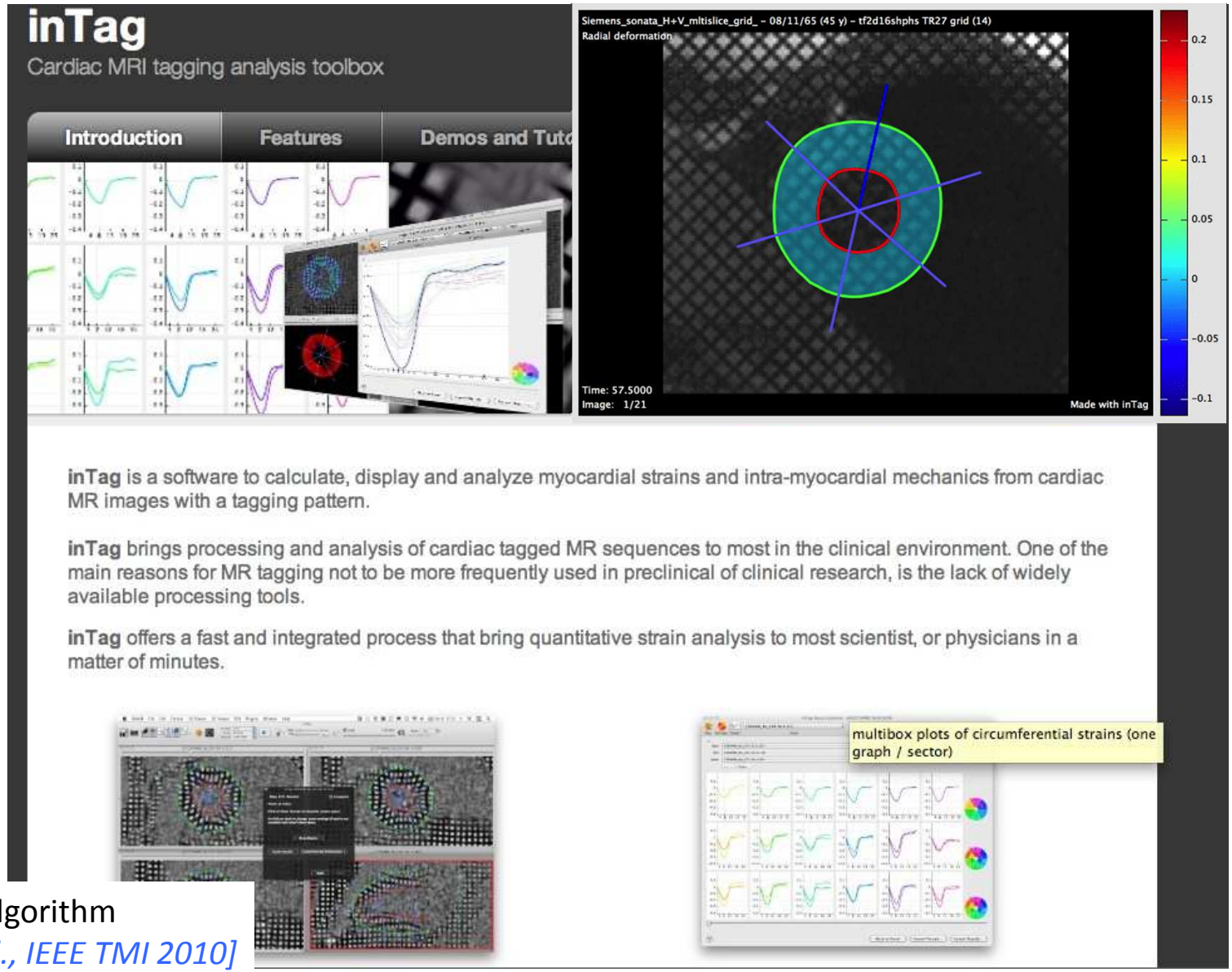


Computed circumferential Strain



HARP is based on phase invariance: for any given point, the harmonic phase is constant with time

[http://www.iacl.ece.jhu.edu/static/harp/]

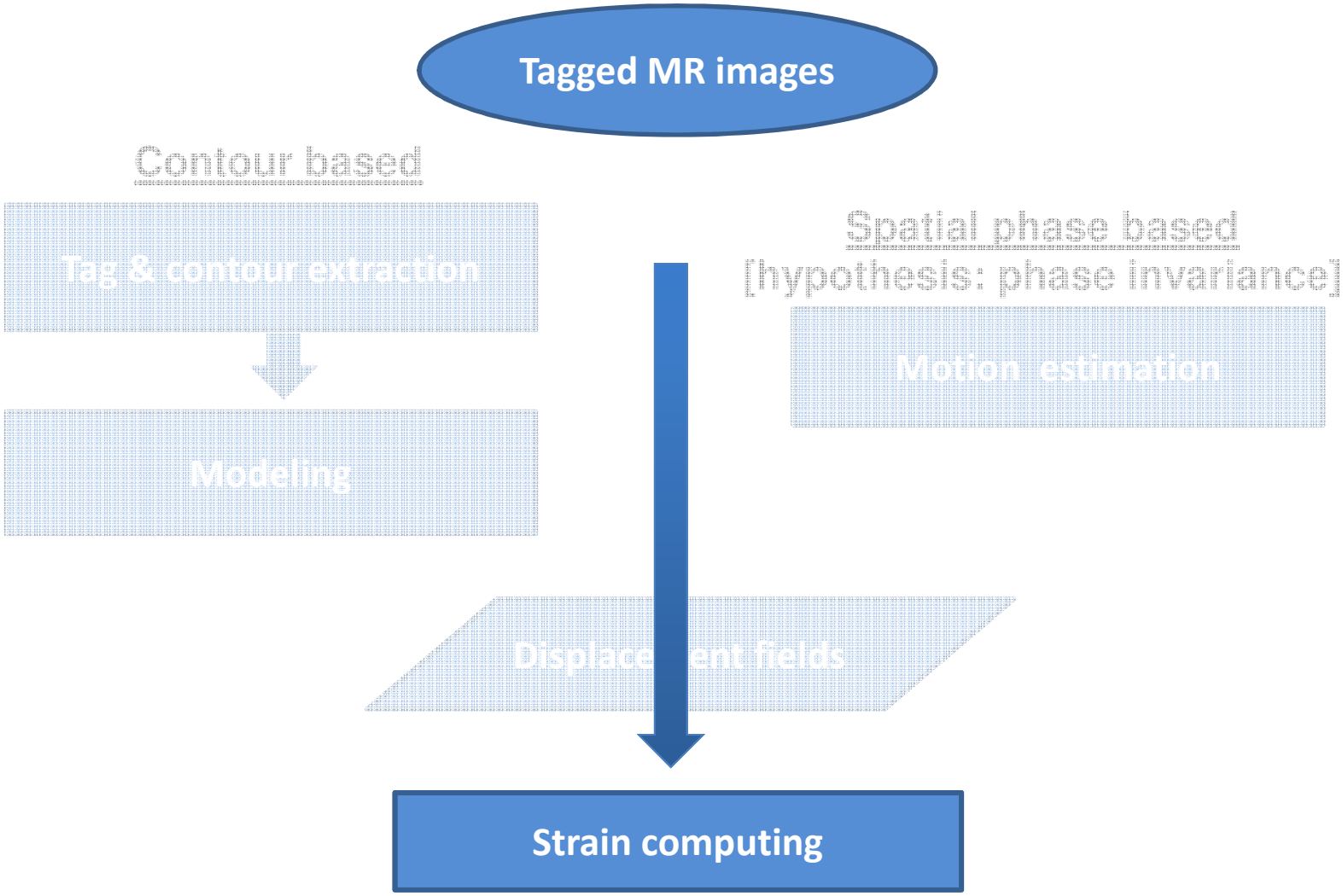


SinMod algorithm
[Arts et al., IEEE TMI 2010]

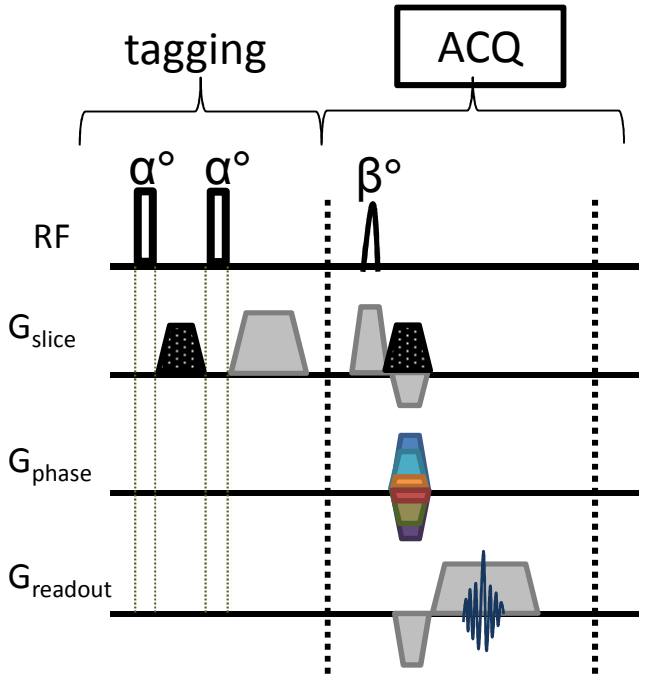
Courtesy of Dr. P Clarysse, CREATIS

http://www.creatis.insa-lyon.fr/inTag/

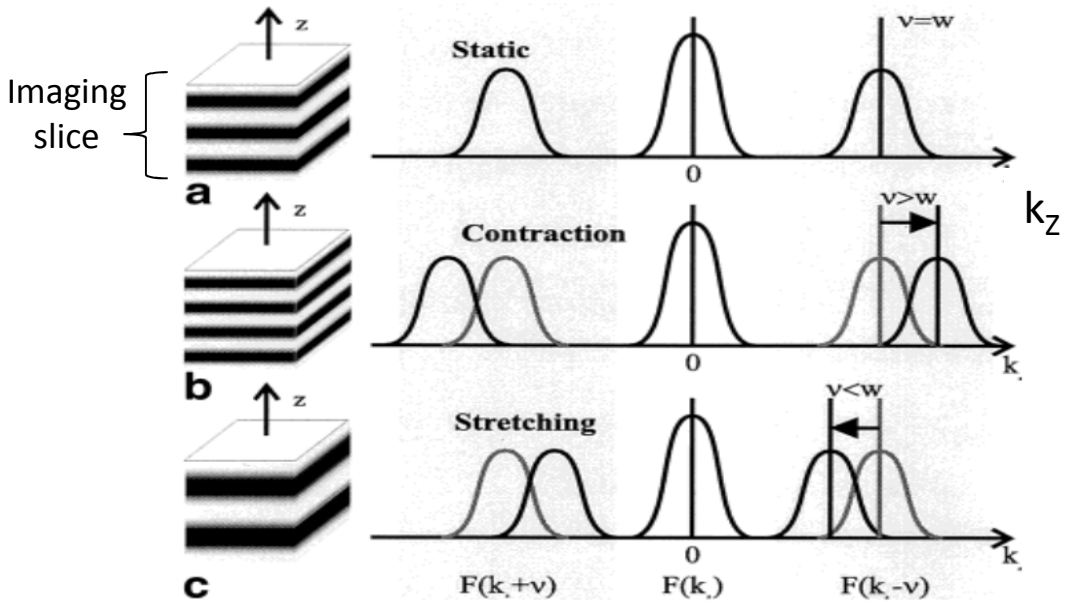
Post-processing for advanced MR Tagging



Strain ENCoding (SENC)

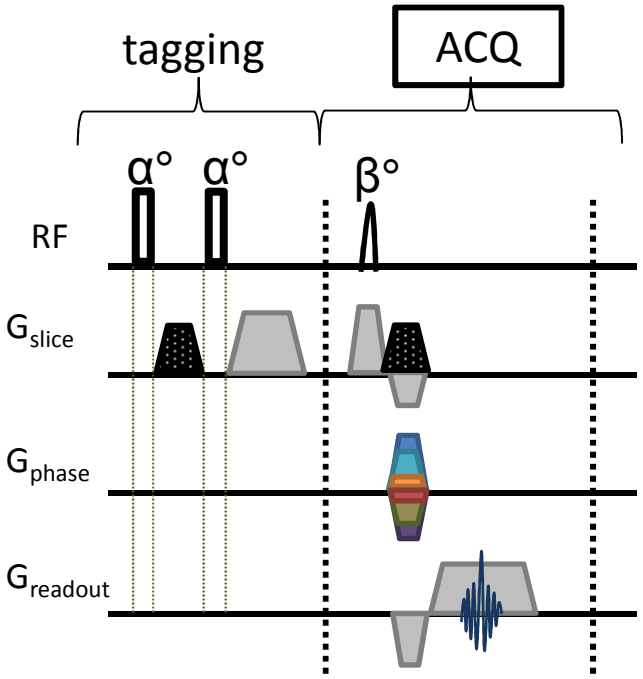


SENC Pulse sequence

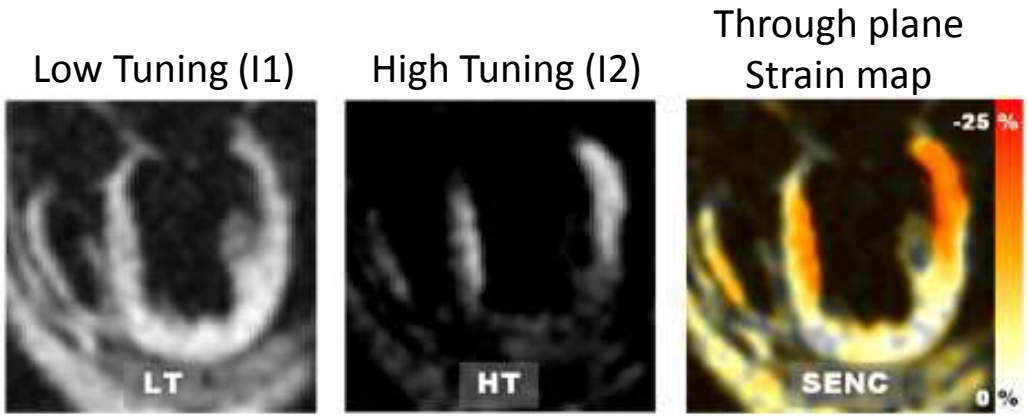


[Osman et al, *MRM* 2001]

Strain ENCoding (SENC)



SENC Pulse sequence



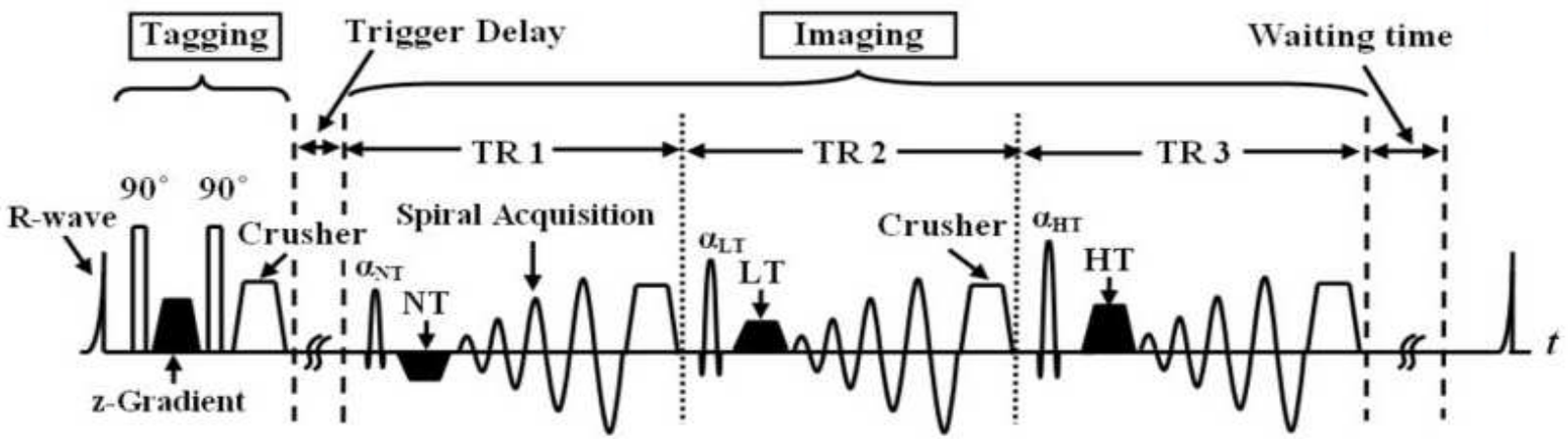
$$demodulation\ frequencies:$$
$$f(x,y;0) = f_{d1}; f_{d2} = f_{d1} + \frac{1}{L}; L - \ slice\ thickness$$

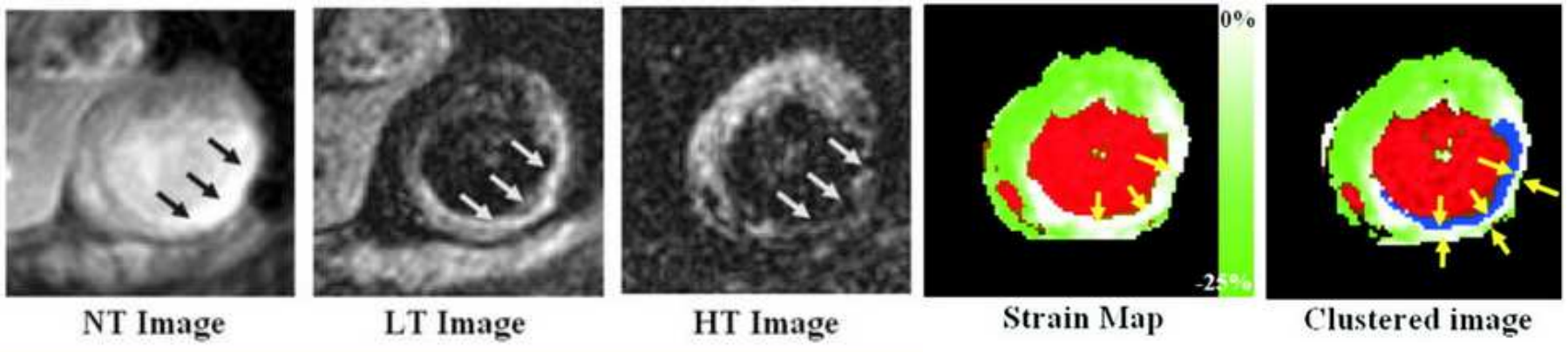
$$\hat{f}(x,y;t) = \frac{I_1(x,y;t)f_{d1} + I_2(x,y;t)f_{d2}}{I_1(x,y;t) + I_2(x,y;t)}$$

$$Strain: \quad \varepsilon(x,y;t) = \frac{d(t)-d(0)}{d(0)} = \frac{f(x,y;0)}{f(x,y,t)} - 1$$

[Osman et al, *MRM* 2001]

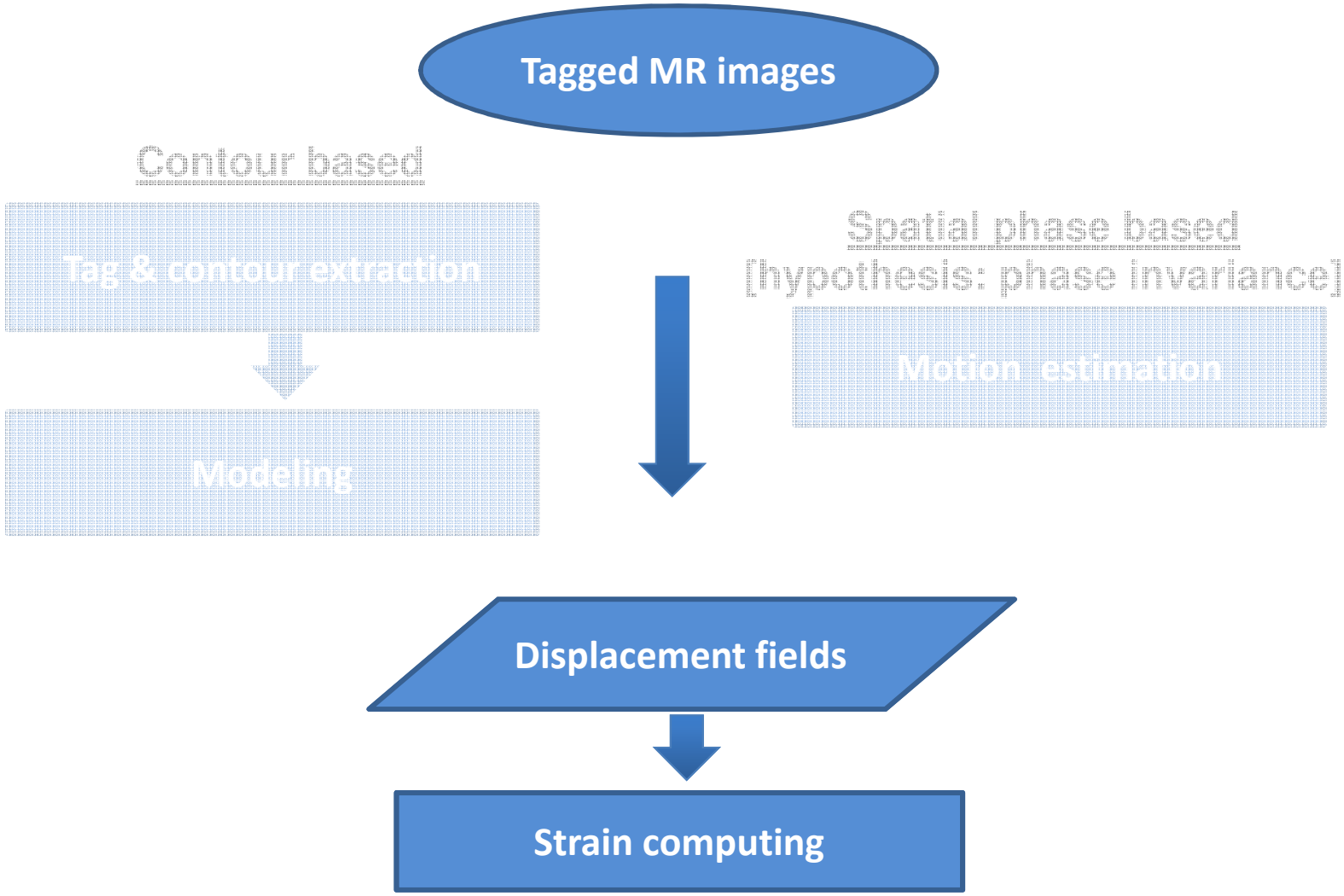
Composite Strain encoding (C-SENC)



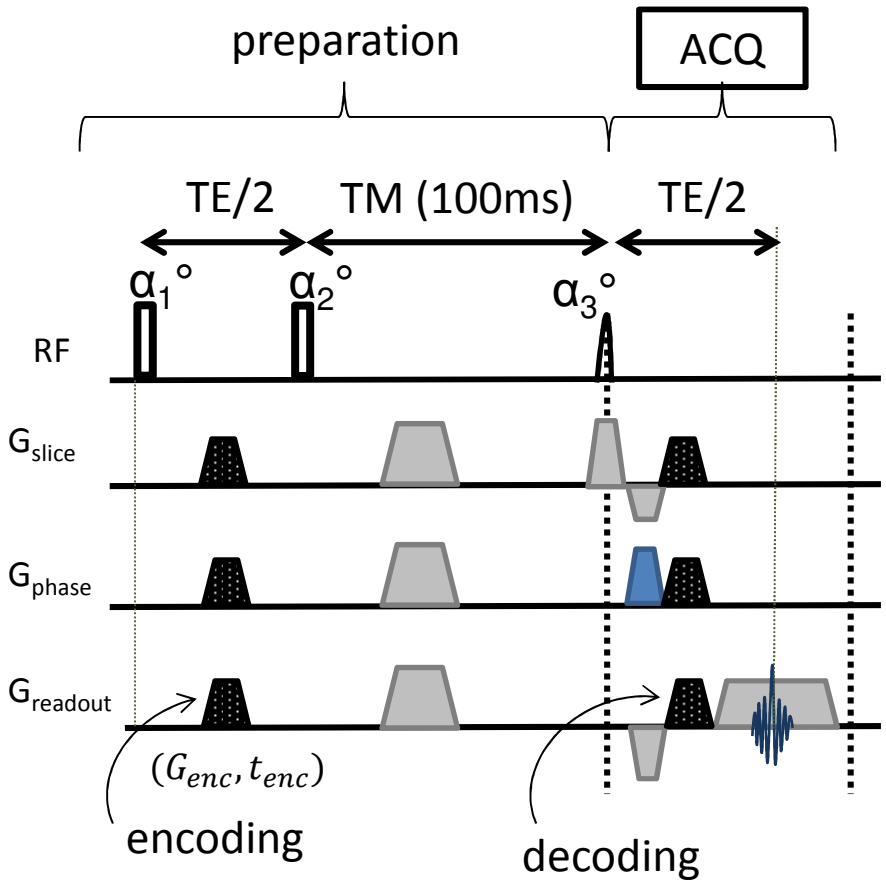


[Ibrahim ES et al, *JMRI* 2008]

Post-processing for advanced MR Tagging



Displacement encoding with stimulated echoes (DENSE)



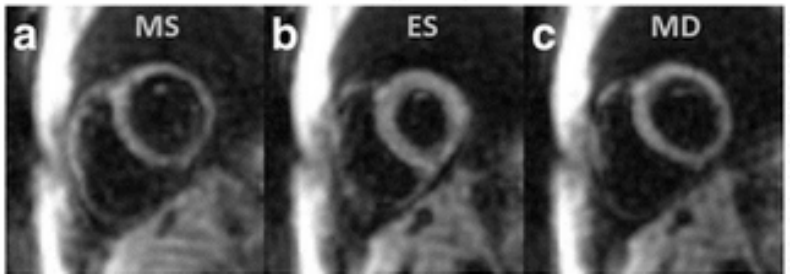
DENSE Pulse sequence

$$\varphi_1 = \gamma_H G_{enc} t_{enc} \Delta x$$
$$\varphi_2 = \gamma_H G'_{enc} t_{enc} \Delta x$$

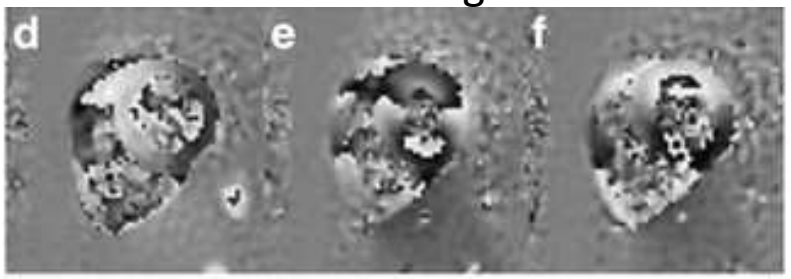
$$\Delta\varphi = \gamma_H t_{enc} (G_{enc} - G'_{enc})\, \Delta x,$$

Δx – displacement during TM

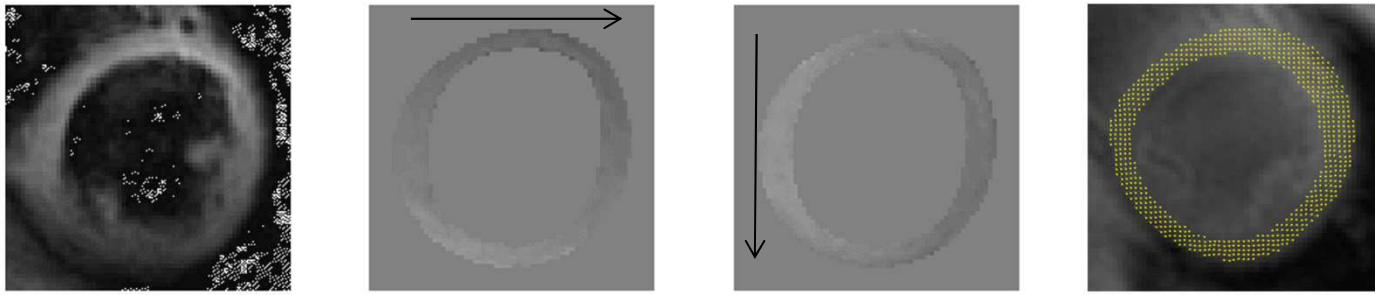
Magnitude images



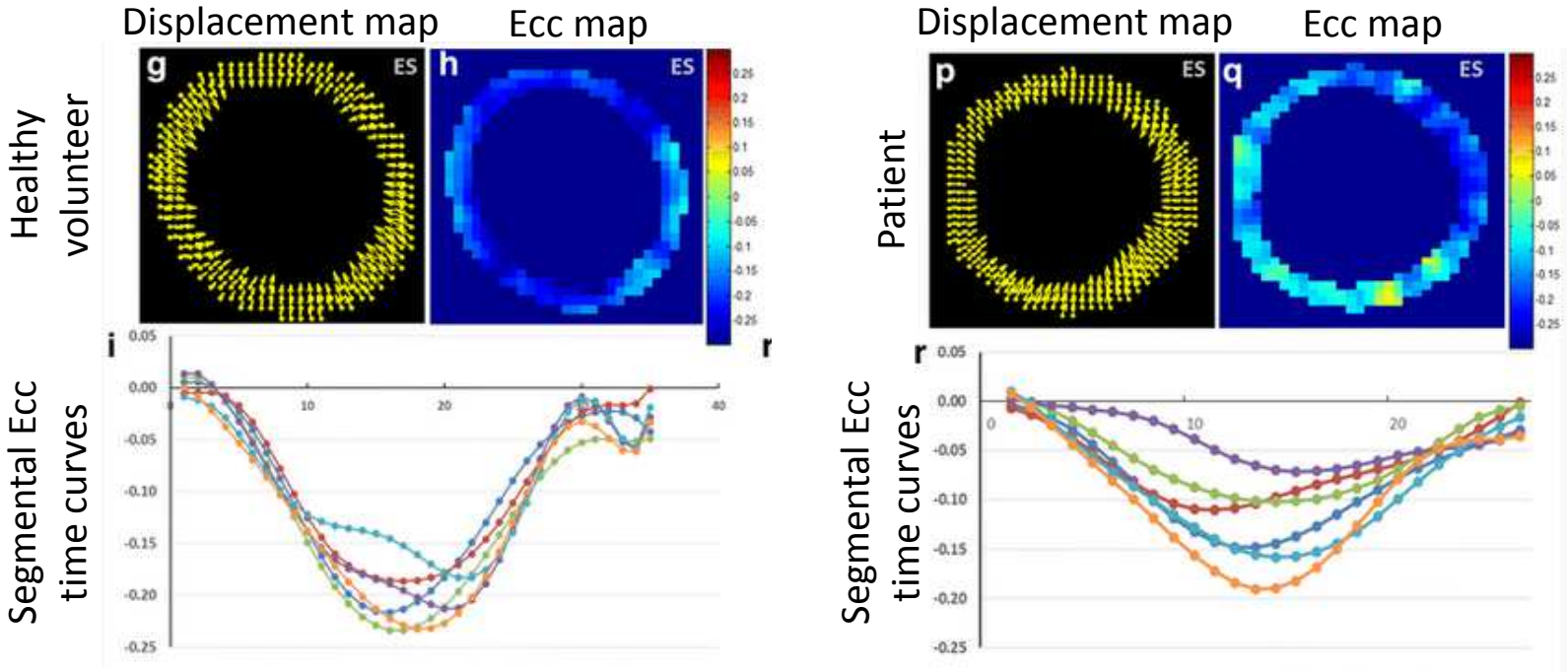
Phase images



Analysis of DENSE MRI



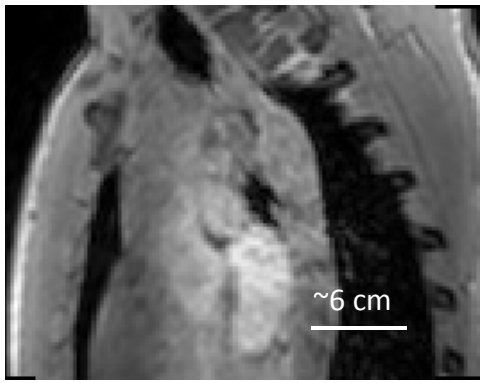
[http://www.fornwaltlab.com/research.html]



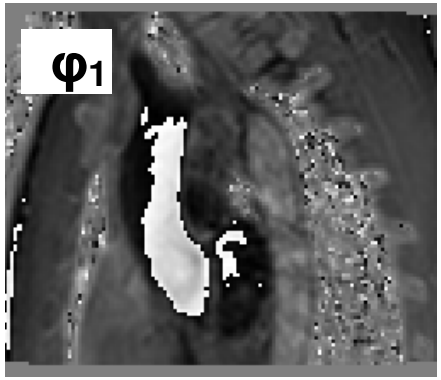
[Chen X et al, *JCMR* 2016]

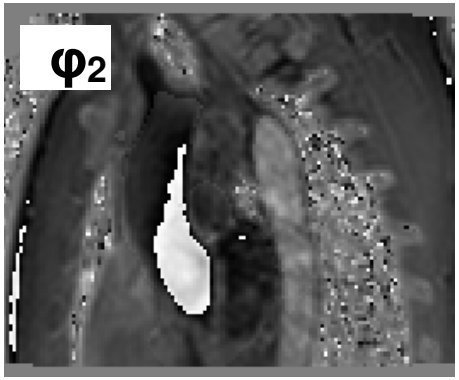
Phase Contrast MRI (PC-MRI)

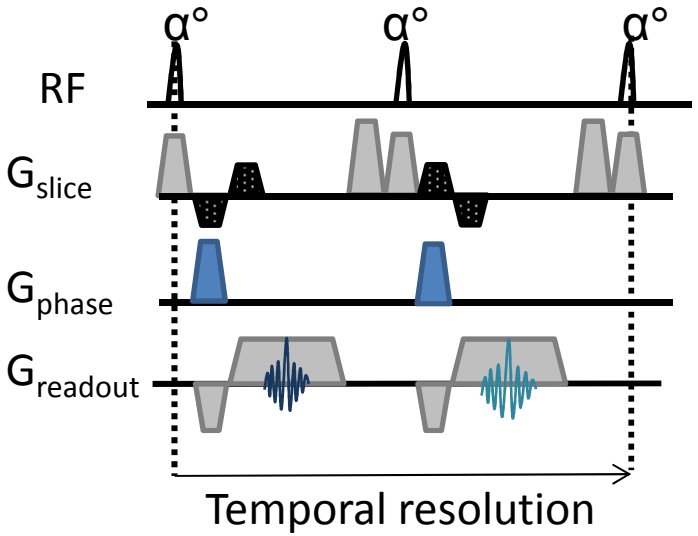
Magnitude image



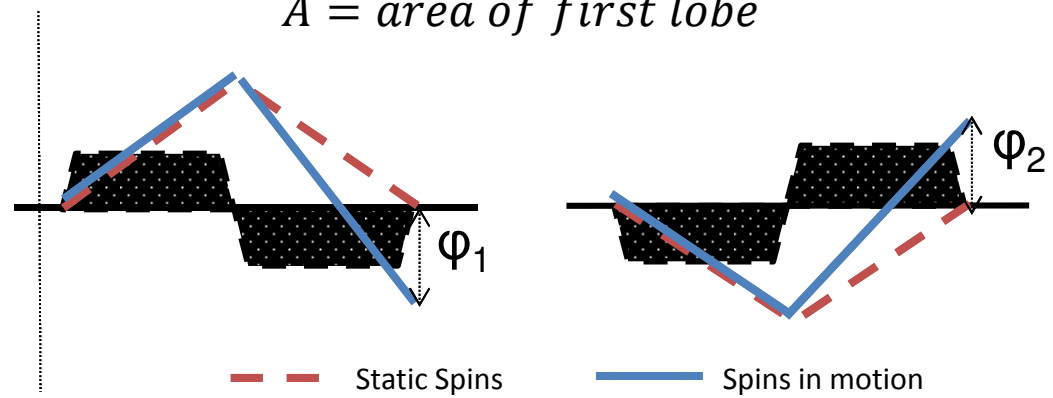
Phase image







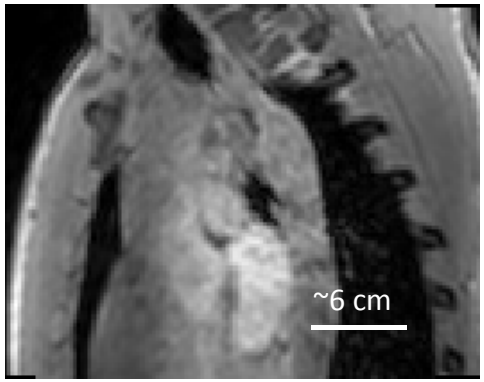
$$\varphi_1(v) = -\gamma v M_1, M1 = AT,$$
$$A = area\ of\ first\ lobe$$



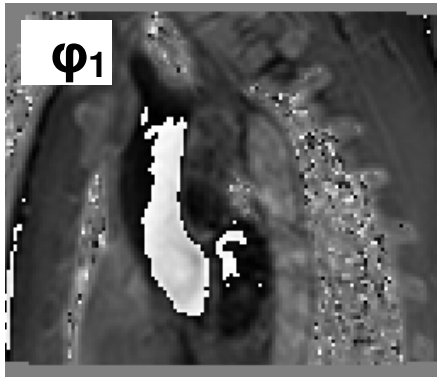
[Moran PR et al, *MRI* 1984]

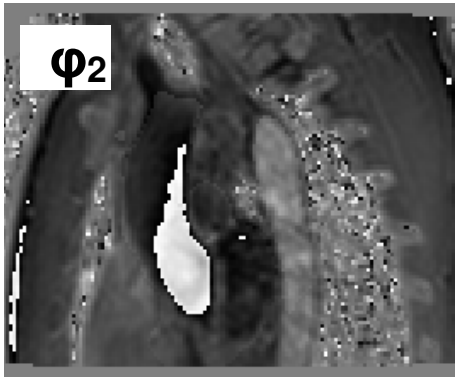
Phase Contrast MRI (PC-MRI)

Magnitude image



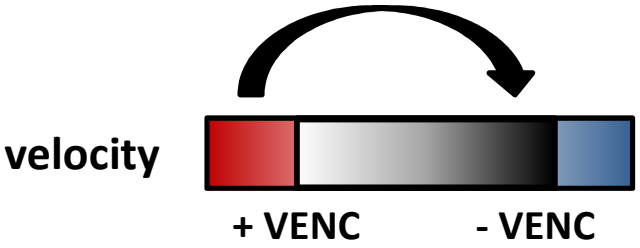
Phase image



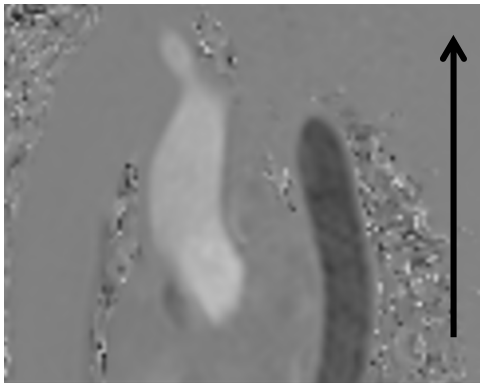


(-)

$$velocity = \frac{\Delta\varphi}{\gamma \Delta M_1} = \frac{\Delta\varphi}{\pi} VENC$$



FH velocity map

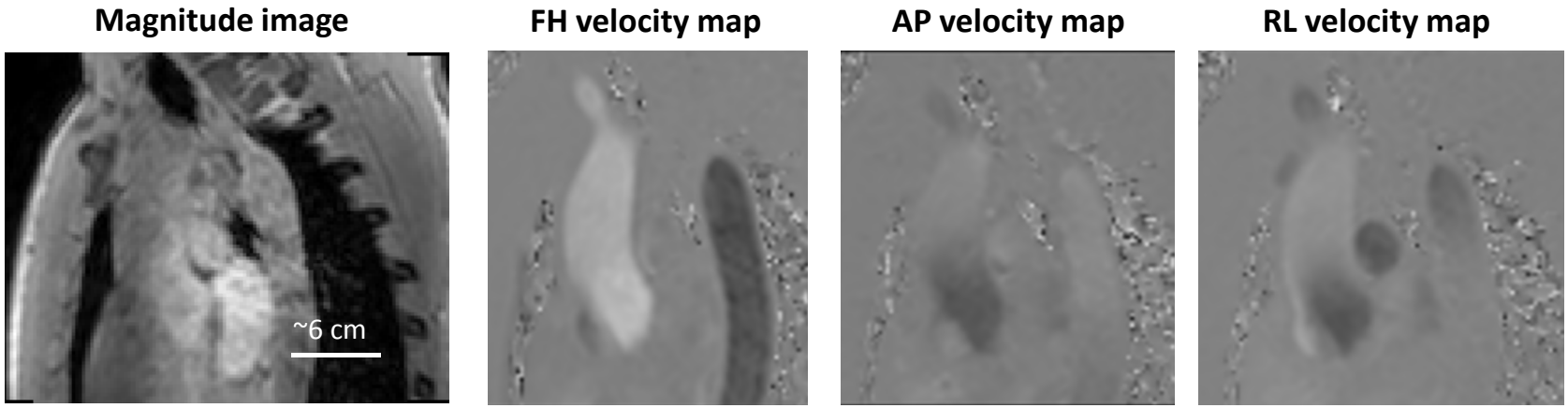


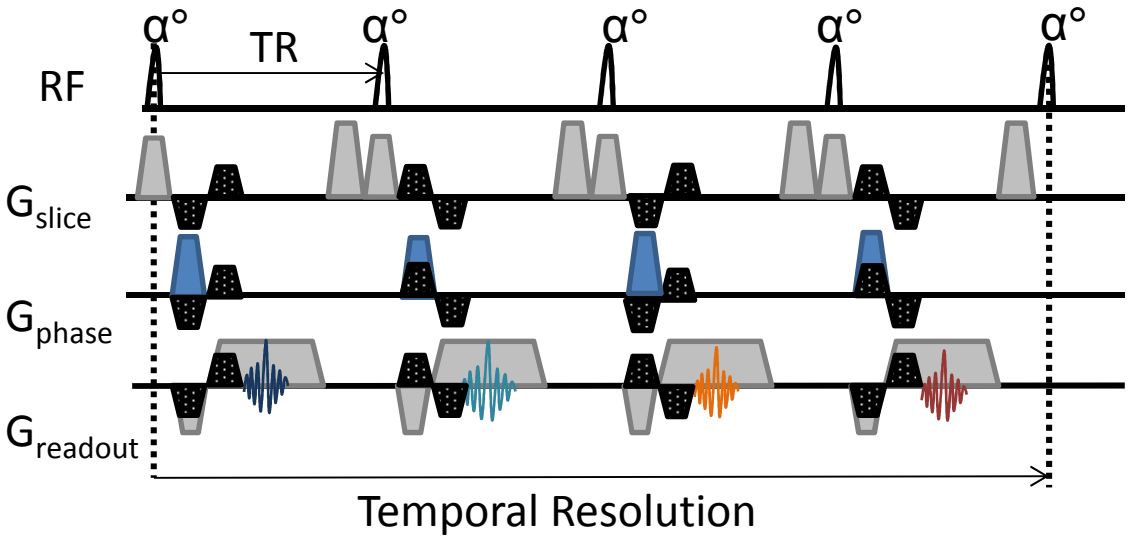
+ VENC



- VENC

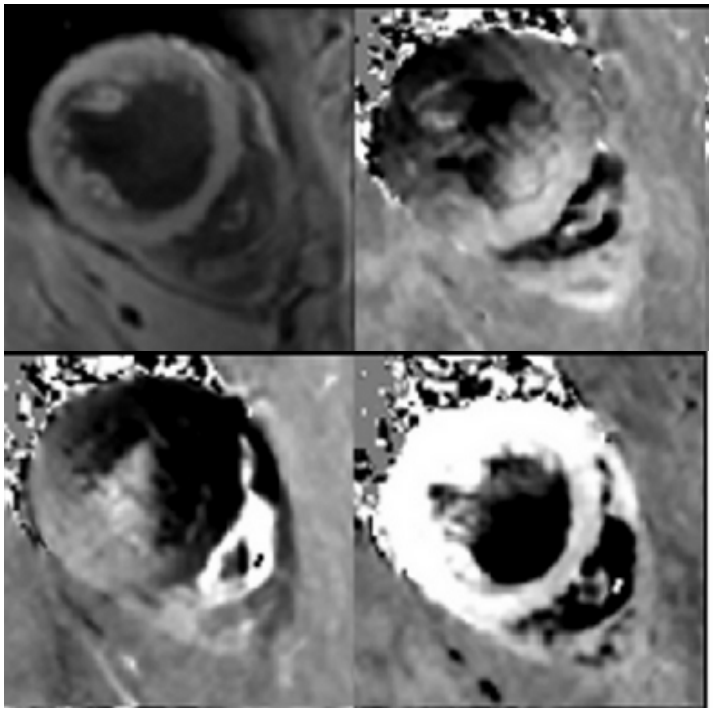
Phase Contrast MRI in 3D (4D Flow)





- A minimum of 4 acquisitions to measure 3 projections of the velocity vector
- Different types of encoding:
  - Hadamard
  - 1 Reference + 3 bipolar directions
  - …

Myocardial tissue phase mapping



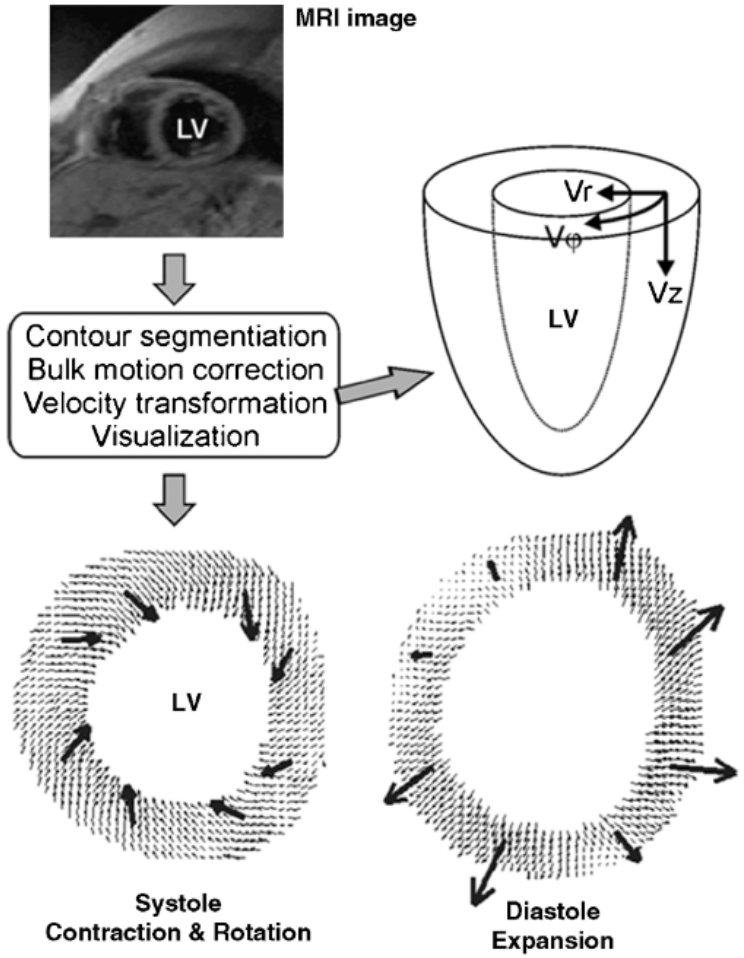
[Lutz et al, *JCMR* 2011]

Limitation for cardiac tissue mapping:

$$velocity = \frac{\Delta\varphi}{\gamma \Delta M_1}$$

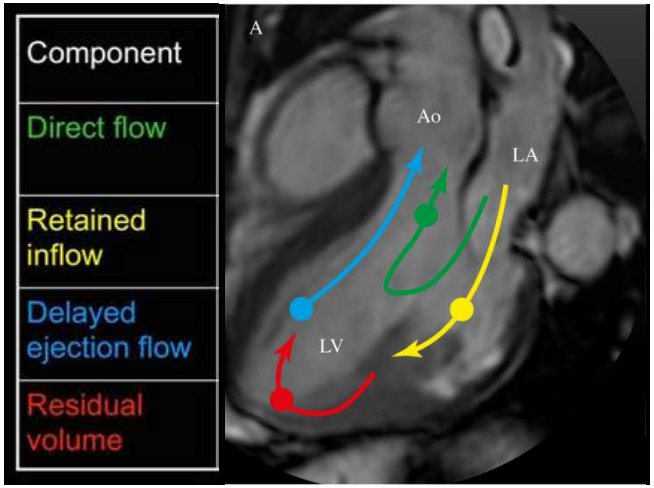
VENC = 150 cm/s -> TE ~ 2 ms

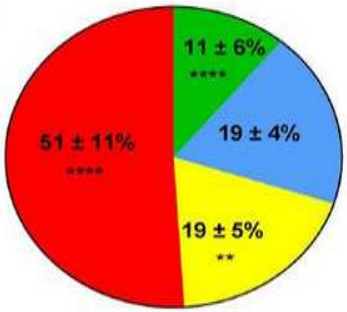
VENC = 20 cm/s -> TE ~ 4 ms



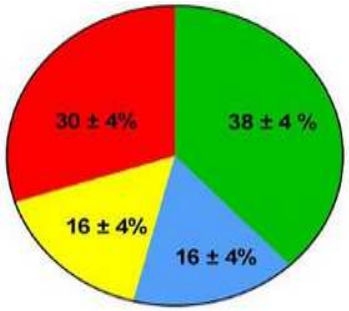
[Jung et al, *EJCardioThorcSurg*2006]

Assessment of LV function using 4D Flow

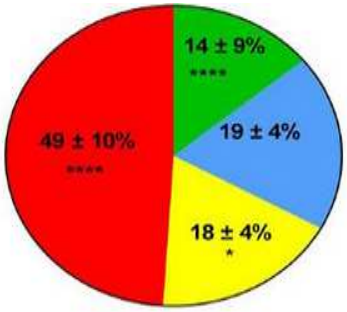




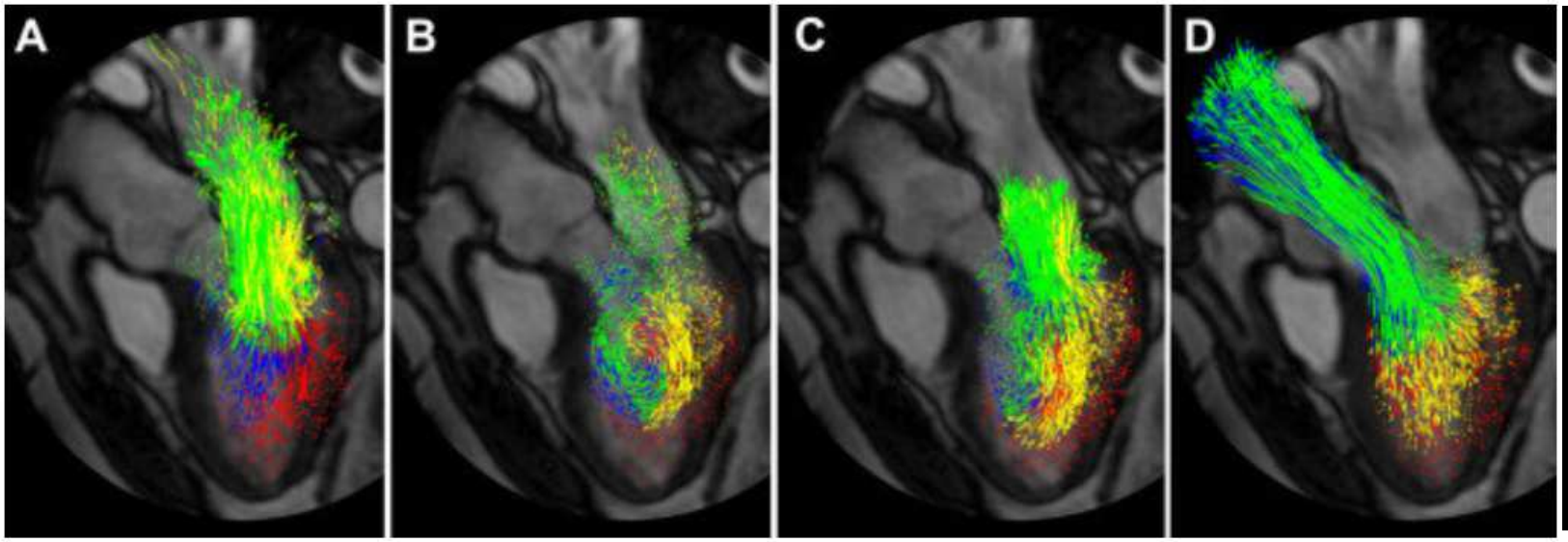
Dilated CardioMyopathy



Healthy Volunteers



Ischemic Heart Disease



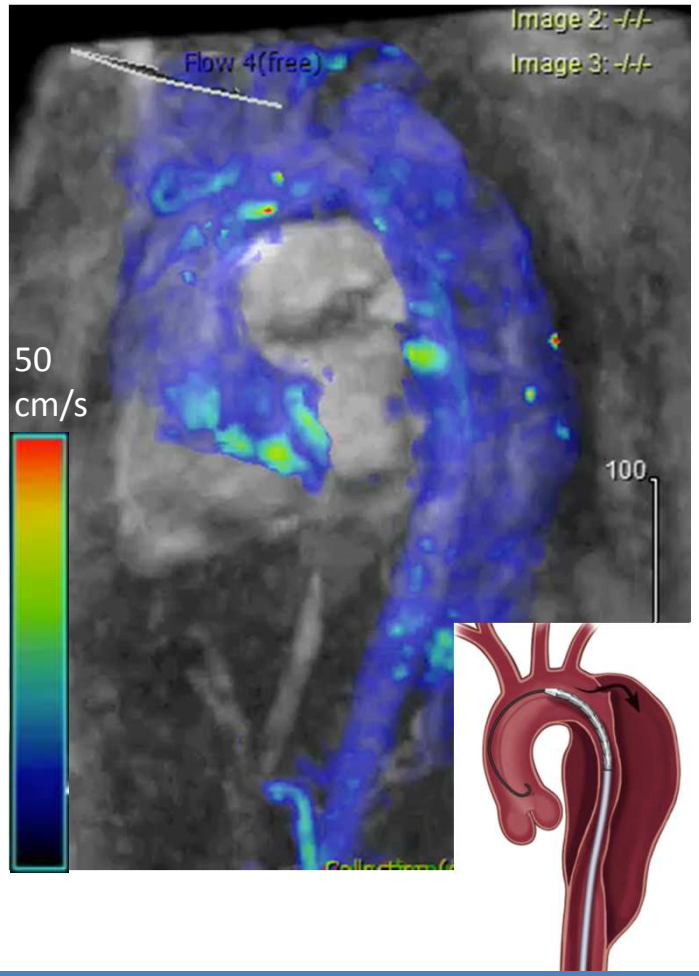
Intra-cardiac flow - 61 year old healthy volunteer: filling of the LV (A), diastasis (B), atrial contraction (C), and peak systole (D).

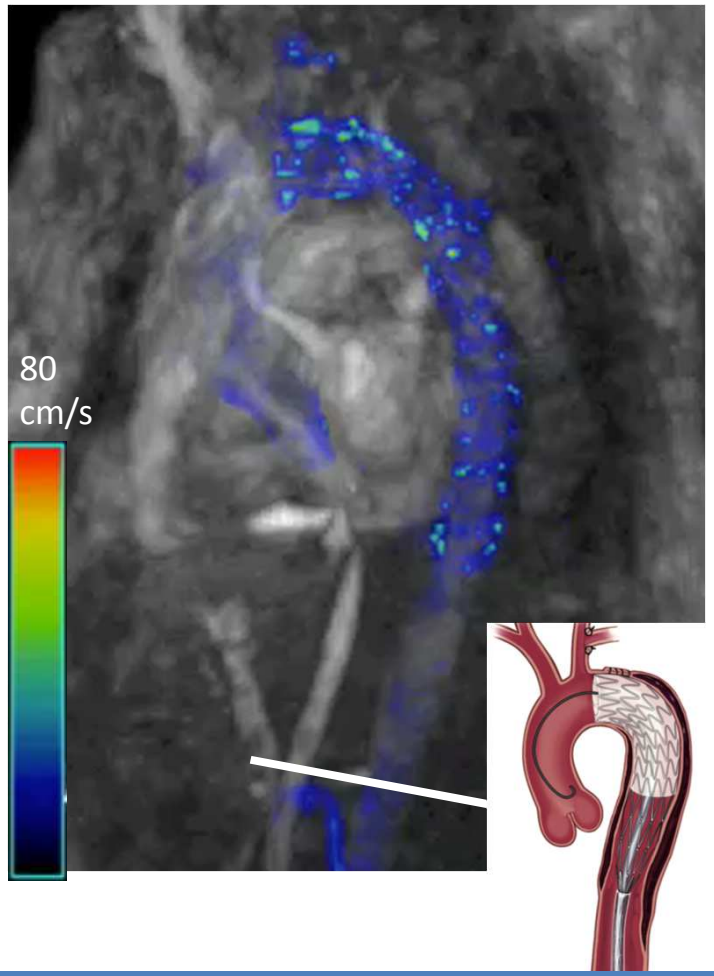
[Eriksson J et al, *JCMR* 2010; Svalbring E et al, *PlosOne* 2016; Stoll V et al, *JCMR* 2016]

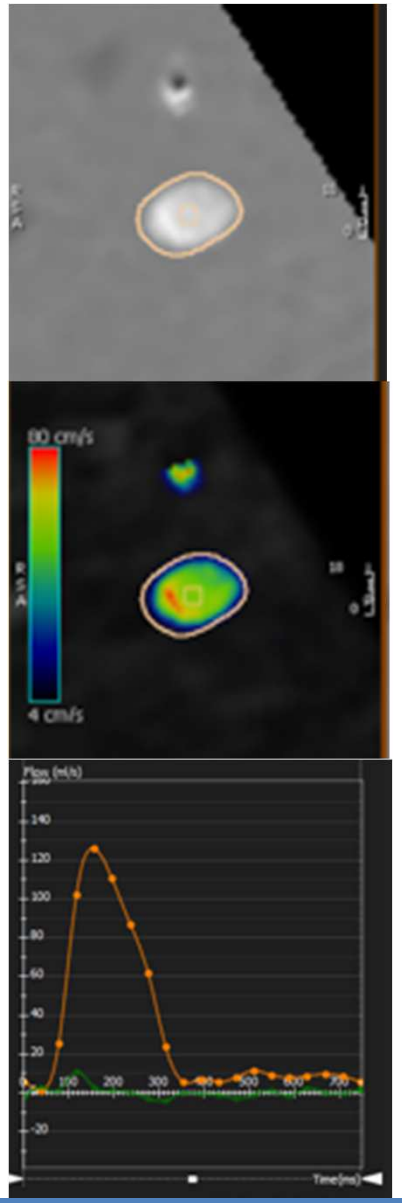
Treatment follow-up in type B aortic dissection

Pre-treatment

Endo-prosthesis placement







Take home messages

MRI basics:

- MRI makes use of the magnetic properties of nuclei with uneven number of protons => magnetic dipole
- Most often we will use the water protons to create images
- The contrast in MR images
  - depends on the specific tissue relaxation rates and proton density
  - Can be further controlled by magnetization preparation modules

Motion measurements:

- Global measurements of heart function are based on dynamic morphology images
  - Ejection fraction, Stroke volume,…
- Global measures may be insensitive to alterations in regional performance

Take home messages

Motion measurements:

- Assessment of regional performance –> strain computations
- Three types of approaches to obtain cardiac strain from MRI:
  - Generation of tissue markers to estimate displacement fields: Tagging
  - Direct measure of displacement fields: PC-MRI, DENSE
  - Direct measure of Strain: SENC

- MR tagging
  - Uses magnetization preparation to create a pattern in the magnitude
  - Requires cumbersome post-processing to estimate displacement fields from which the strain is then computed
  - Is the reference technique, used on the largest number of patients
  - Never became part of clinical routine

Take home messages

Motion measurements:

- PC-MRI
  - Motion information is encoded in the phase of the MR signal
  - Not adapted for measuring slow moving tissue
  - Provides rich information on blood flow in vascular diseases
- DENSE
  - Overcomes the limitation of PC-MRI for tissue motion
  - Simpler post-processing compared to Tagging
- SENC
  - Directly encodes the strain in the amplitude of two images
  - Straightforward and fast post-processing

Thank you