S. David Smith

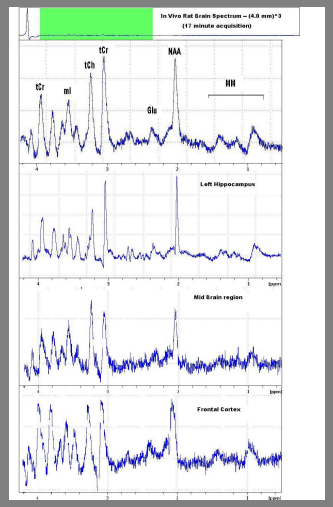
Imaging Scientist and Physicist

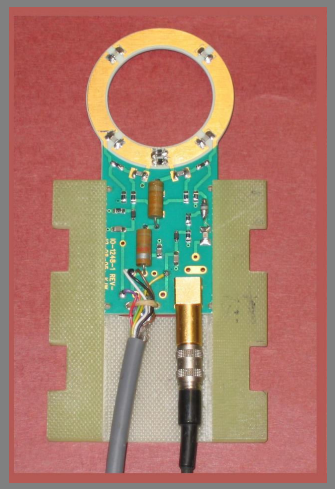
BS, MA and PhD from Columbia University

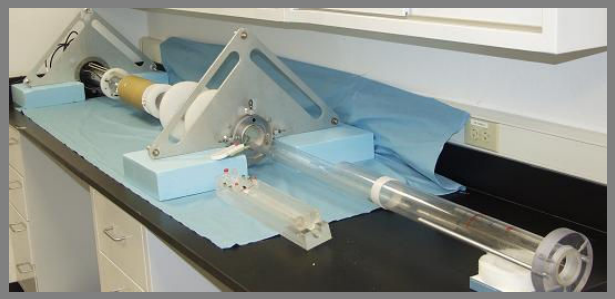
Telephone: (631) 344-7193
Email: SDSmith@BNL.gov

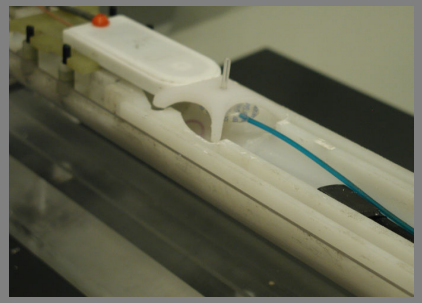
After receiving his PhD in Experimental High Energy Particle Physics, Dr. Smith joined the Physics Department at BNL, enjoying a Post Doctoral appointment specializing in detector design and development. He left Brookhaven in 1982 to take leadership position in private industry for the design and development of Clinical MRI.

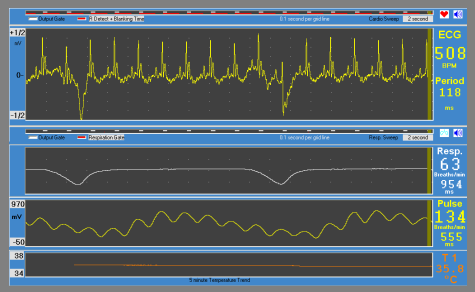
After 25 years of contribution and involvement in virtually aspect of the MRI business, Dr. Smith has returned to BNL providing technical expertise and in depth practical and theoretical understanding of imaging science.

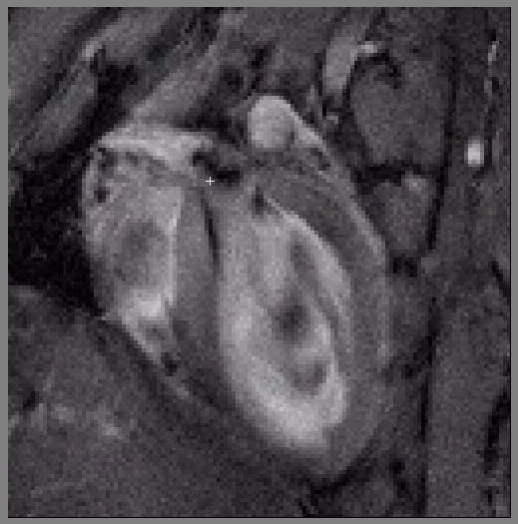


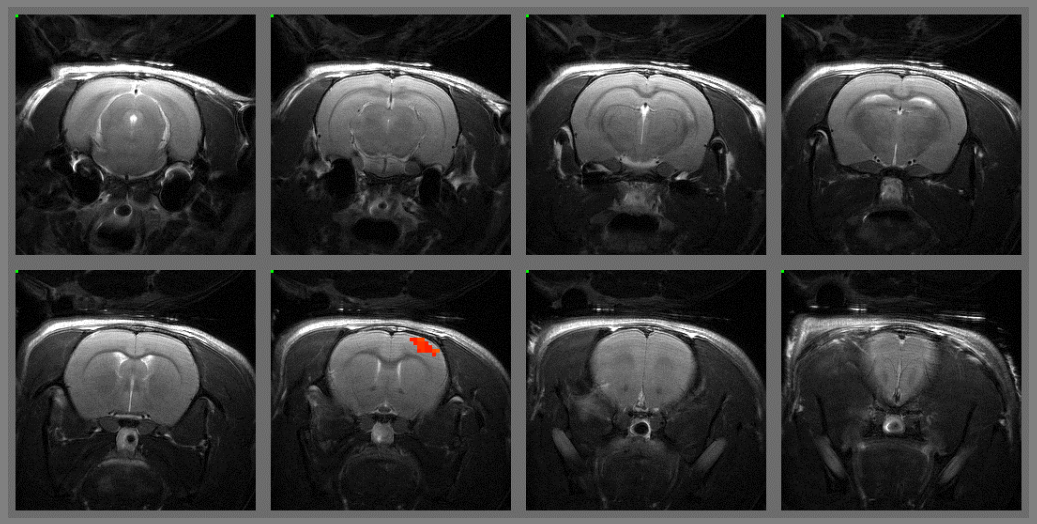


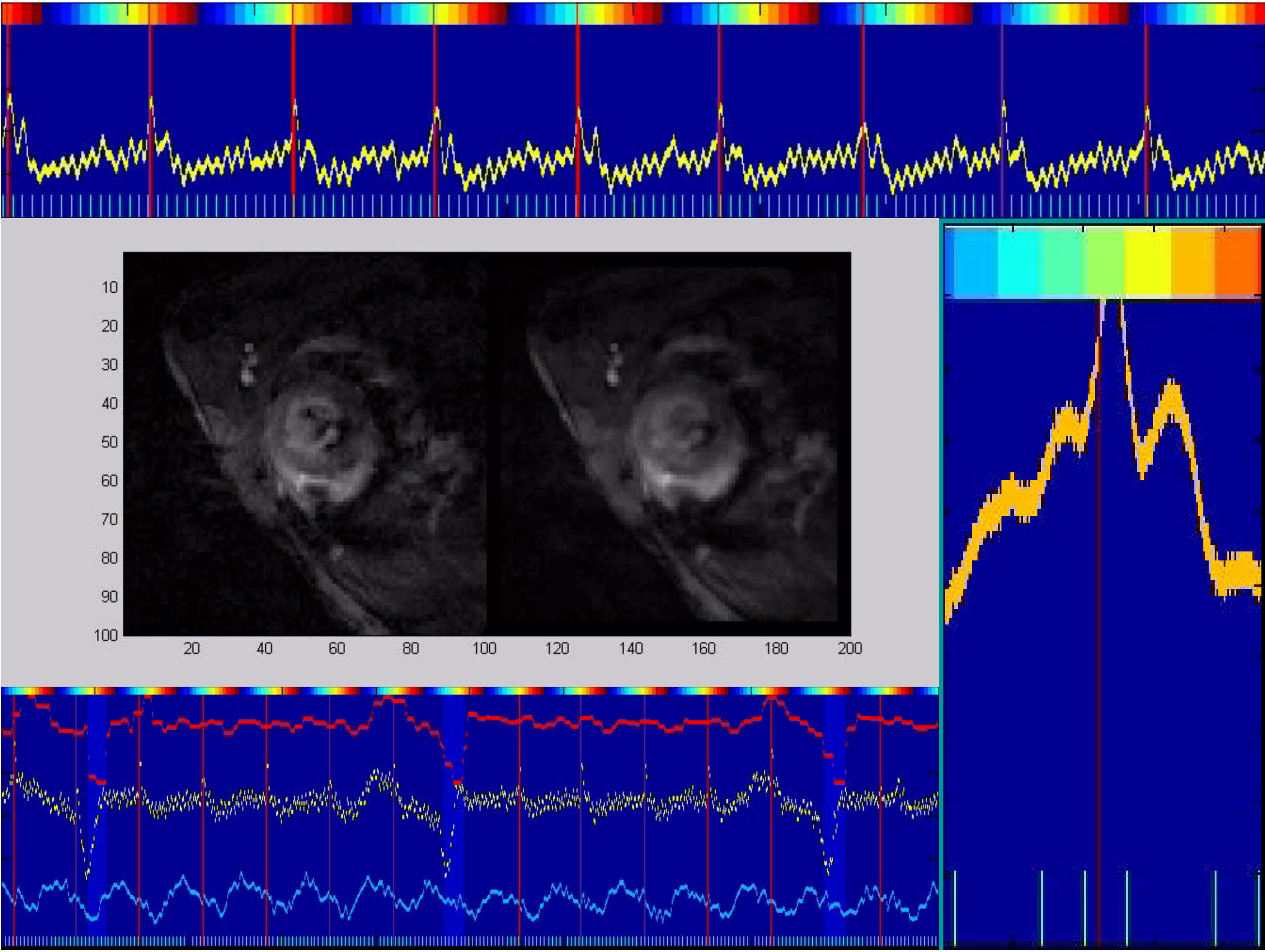











10
20
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140
160
180
200

Critique from prior student reviews:

MORE	LESS
Science	Instrumentation

My conundrum:

Science vs Instrumentation

Theme of the day:

Yesterday's Scientific Discoveries when . . .

applied to create TODAY's INSTRUMENTATION will yield . . .

Tomorrow's New Science!

Remember this:

- Science is accumulated observation
- Observations are made with instruments
- Scientific theories are the flimsiest constructs,
- which may be destroyed with a single observation.

Nuclear Magnetic Resonance

A series of great discoveries

lead to a great instrumentation idea

resulting in new observations and

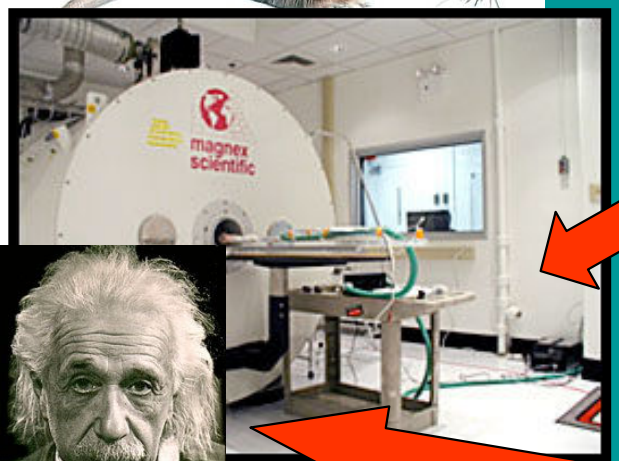
new instrumentation ideas which

yield many more discoveries

. . . and quite a few Nobel Prizes!

MR microscopy, Translational Science & Scientists

"BENCH" ⟷ "BEDSIDE" ⟷ "CURBSIDE"



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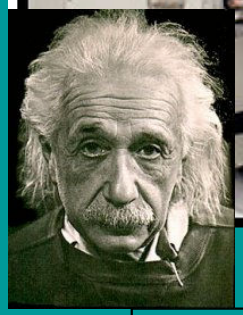
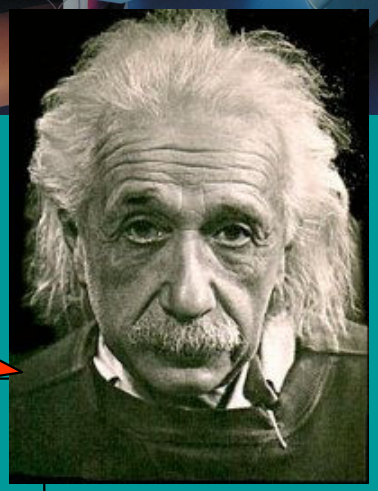
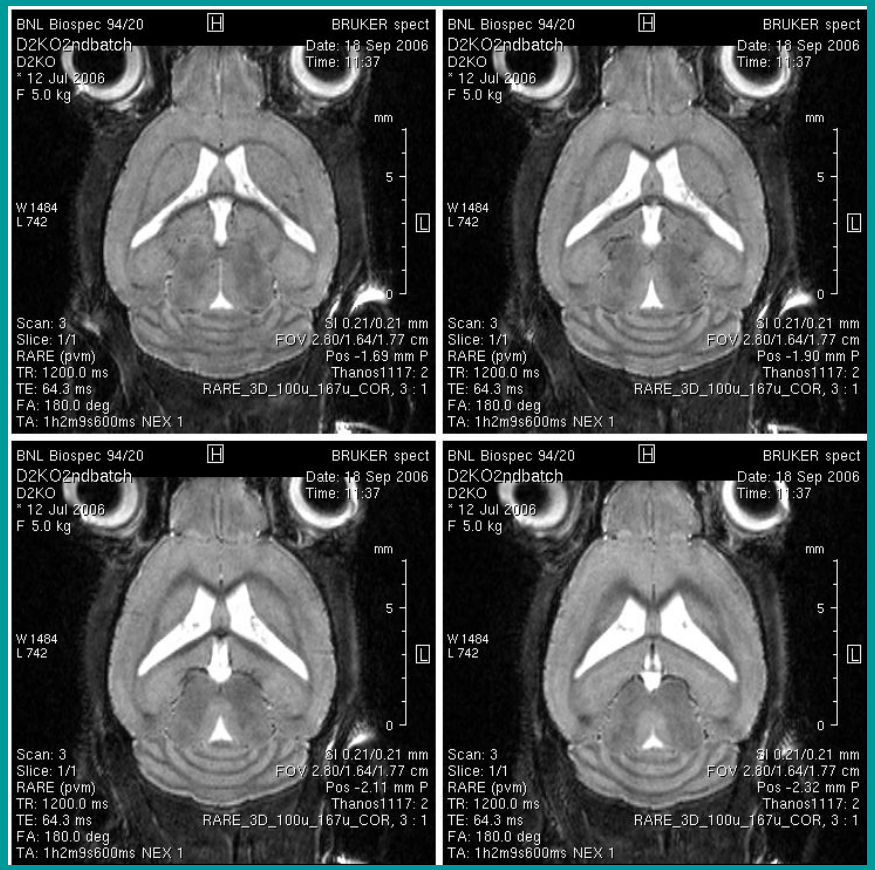


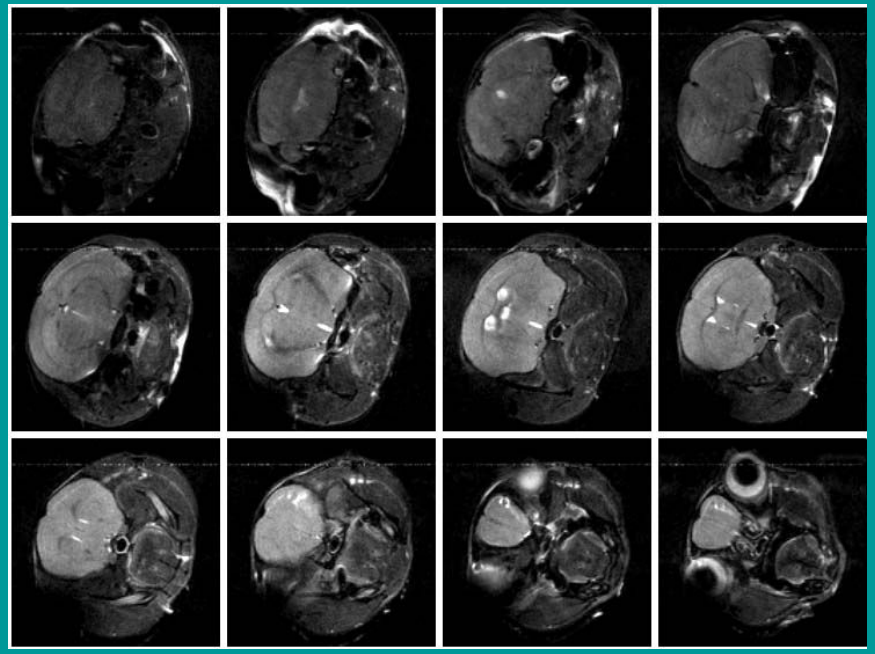


Small animal MR scanners with clinical consoles..

"Translational Scientists"…translating the 'clinical scientist' into the pre-clinical environment and vice versa…

MRI at 23 Tesla





MR Instrumentation & Engineering

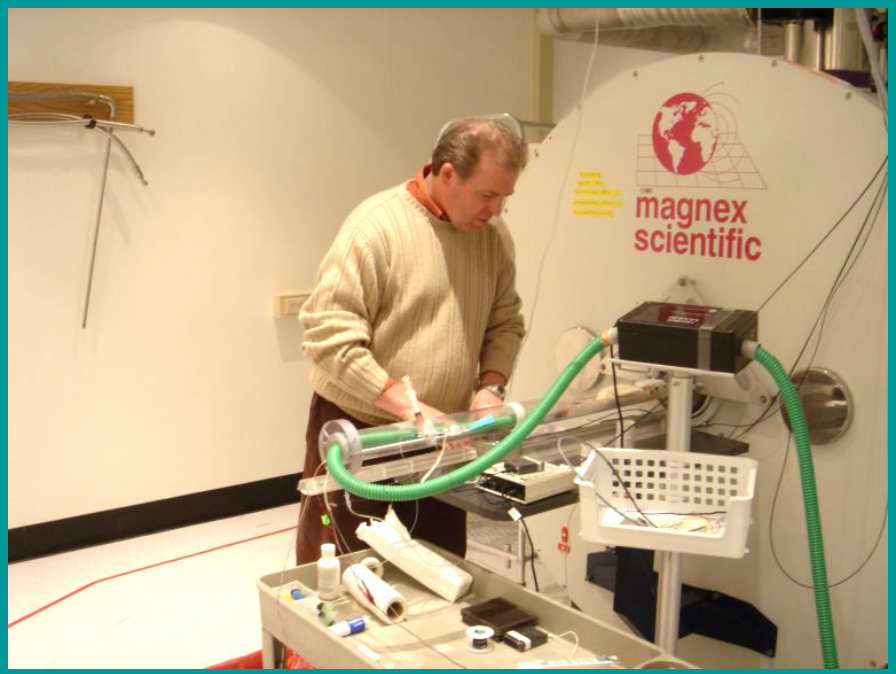
This is the place to be!!

BNL Development Team

S. David Smith, PhD (Medical)

S. Rescia, PhD (Instrumentation)

T. Lambertson (Central Shops)



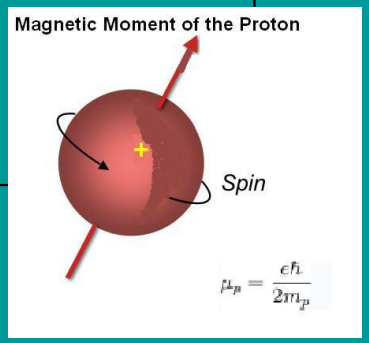
OEM Beta Site Support

SA Instruments, Inc.
Bruker BioSpin NA
SAMBA Instruments (Sweden)

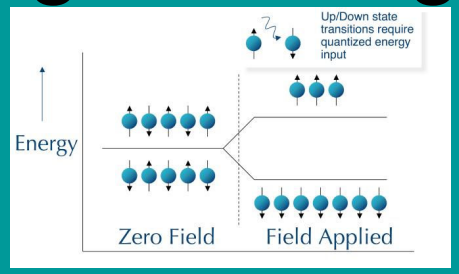
Software Development

In the works . . .

Magnetic moment of the proton



- Quantum Mechanical splitting of Energy states in a magnetic field



- Quantization of electromagnetic field

$$E=h\nu$$

- Stimulated transitions – Resonance!

$$E=h\nu$$

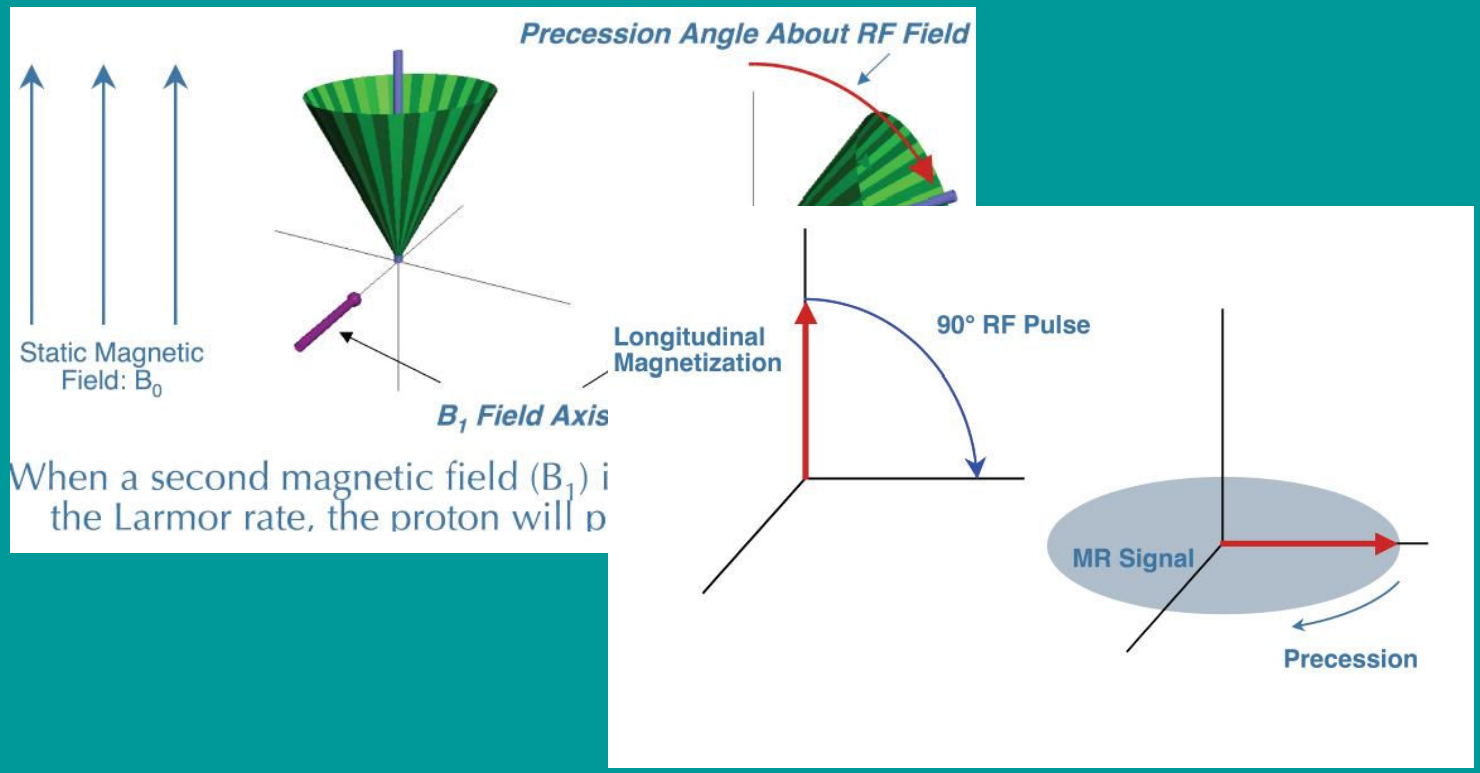
$$E=\mu B$$

$$\mu = e\,h / 2\,m_p$$

$$\nu_r = e / 2\,m_p * B$$

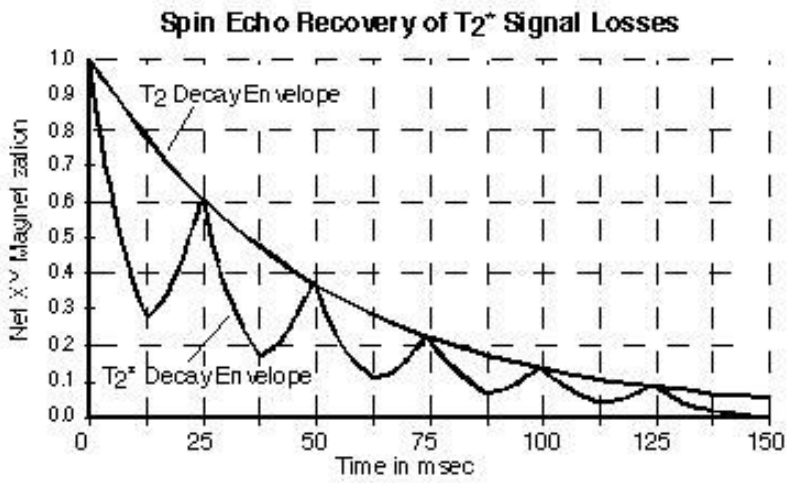
Classical Analog

Larmor Precession:



Hahn Spin Echo

Spin Echoes and the T2 Envelope

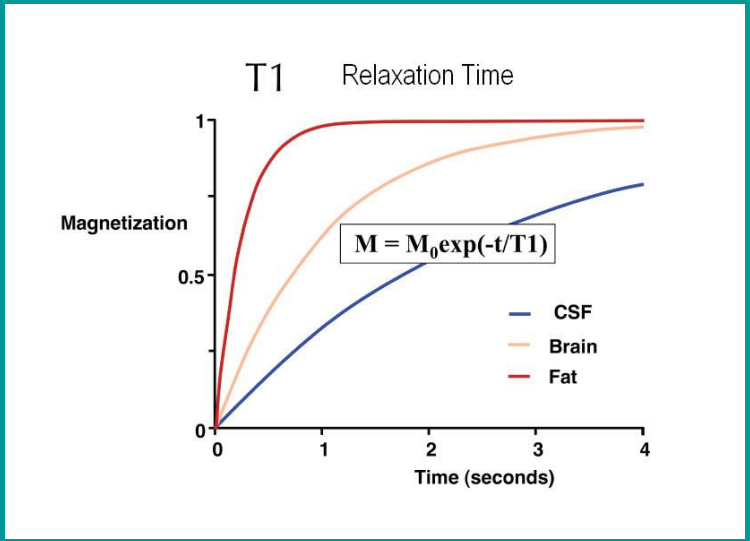


As described above, a 180° pulse can be used to reverse the T2* dephasing process and thereby produce a spin echo. As soon as the spins all come back into phase at the echo time, they immediately start to go out of phase again. A second 180° pulse will generate a second echo. This process can be repeated many times, producing many echos, as long as the pure T2 decay mechanisms have left some signal to work with. We will come back to this topic when we discuss Fast Spin Echo (FSE) imaging.

from:

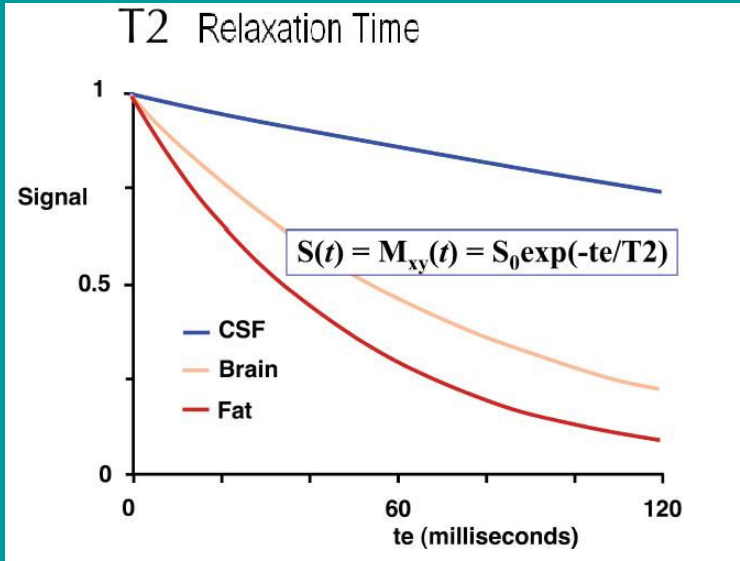
http://www.simplyphysics.com

Relaxation Parameters



Time required to reach a steady state (equilibrium)

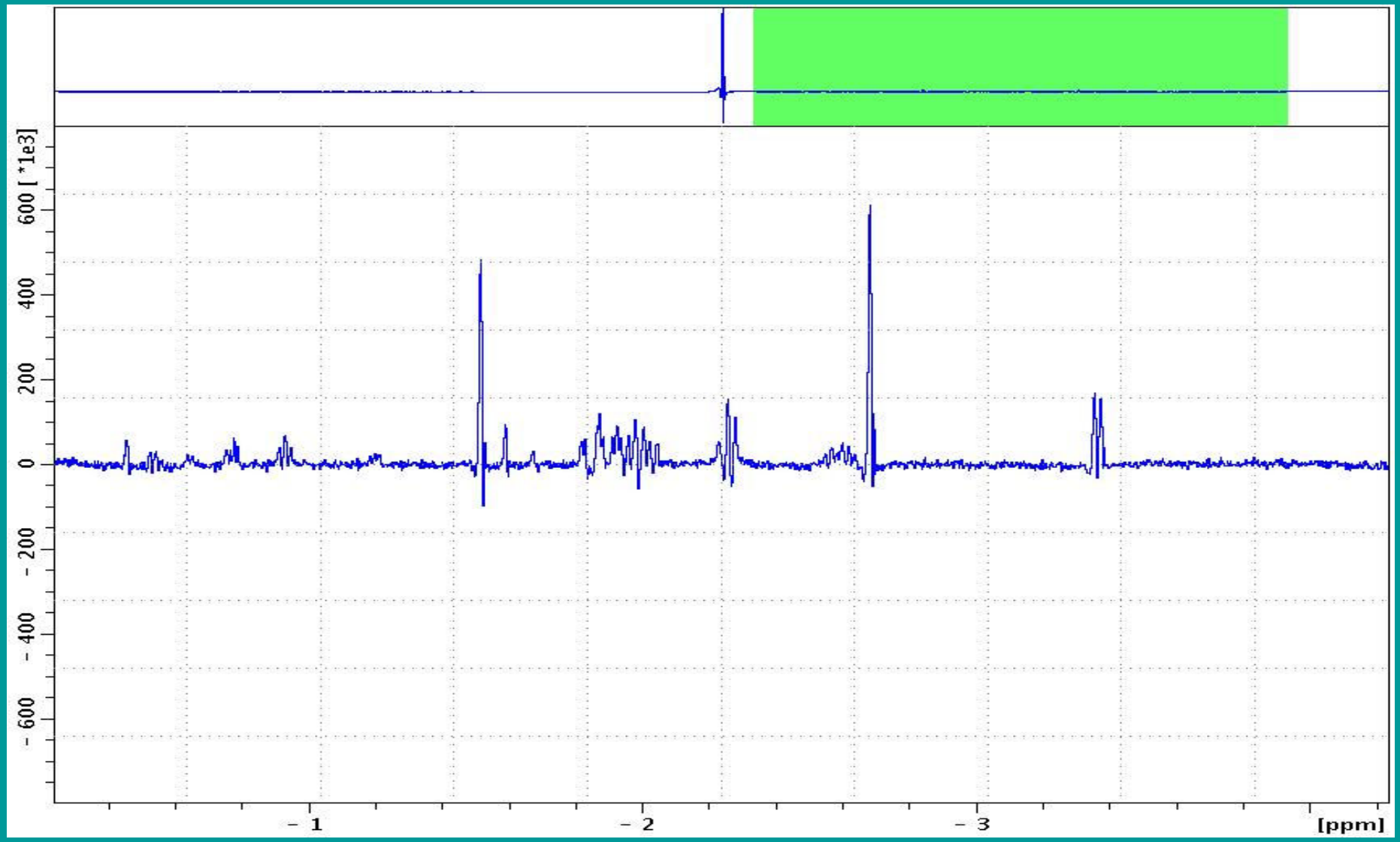
Time until loss of coherence (signal decay)



SPECTROSCOPY:

- Chemical Shift of Larmor Frequency
- Powerful tool for the analysis of complex solutions
- The Chemists choice – long before MRI

Instrument for Chemical Analysis



Magnetic Resonance Imaging

The Gradient Trick

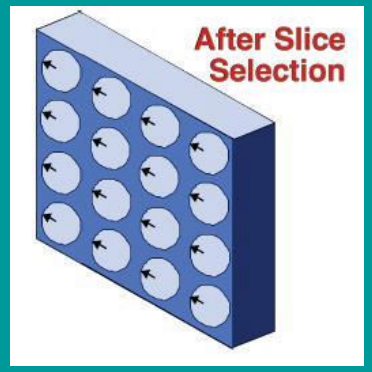
Deliberately destroy field uniformity in order to create one to one mapping between position along one coordinate and resonant (or signal) frequency.

Principle of Fourier decomposition

Any squiggly single valued function can be described uniquely as a sum of SINE waves of various amplitudes, frequencies and phases.

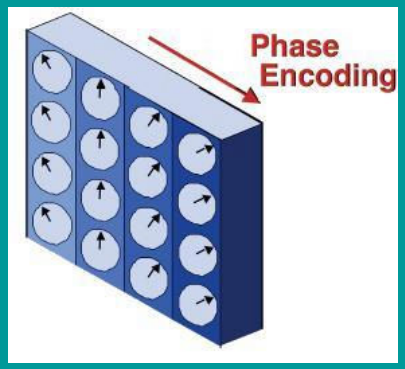
Three ways to use field gradients:

Slice Selection:

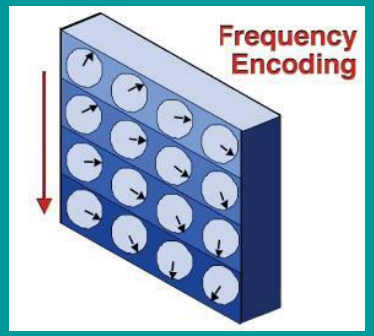


Gradient refocusing

Phase encoding:

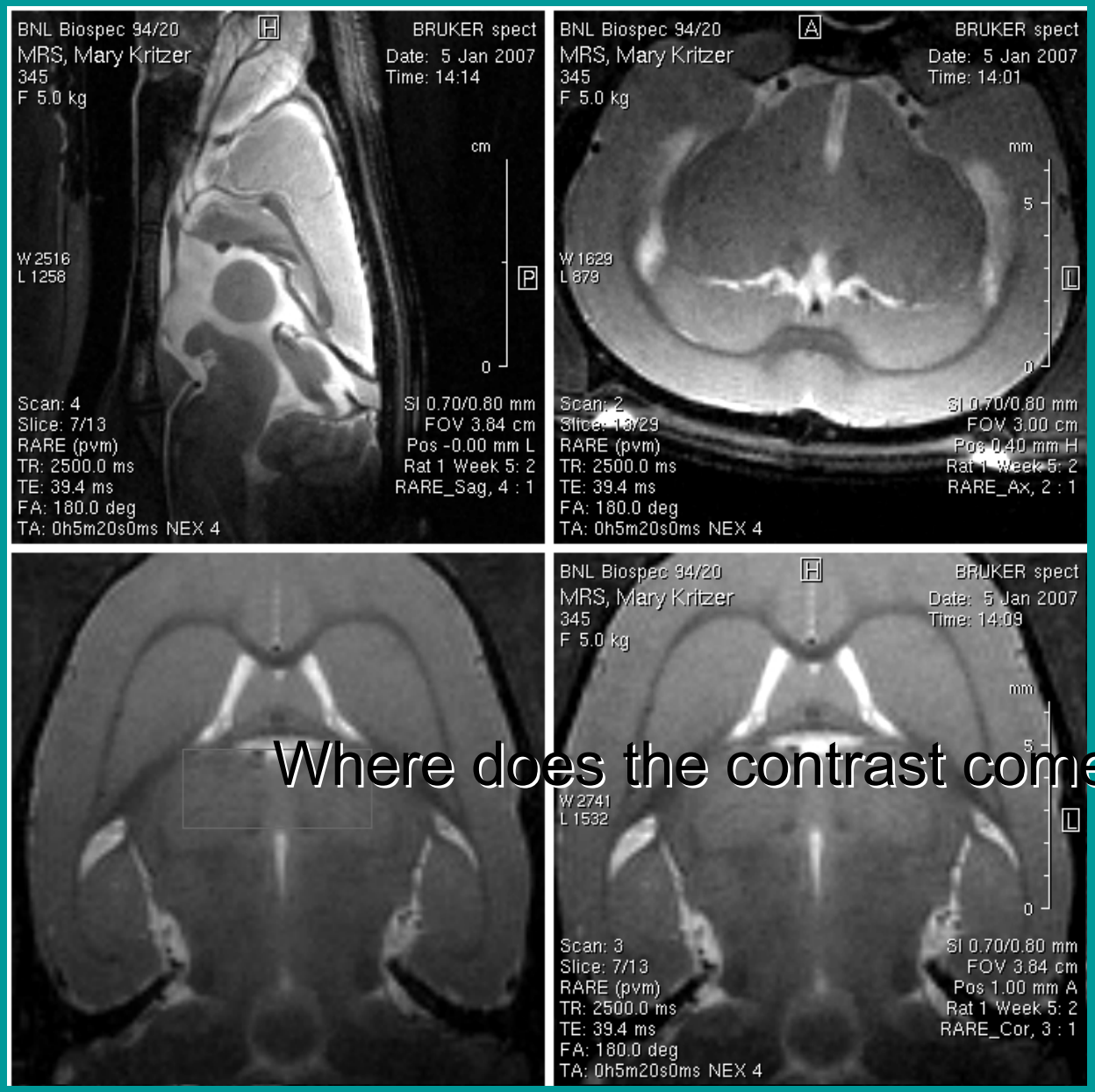


Frequency encoding:



IN VIVO!

What's in an image??



Where does the contrast come from?

T1 and T2 – Chemical Effects

- Relaxation Parameters are affected by disease***
- Image contrast can be changed with changes in TE and TR
- T1 weighted, T2 weighting and much, much more

*** Damadian, R. V. "Tumor Detection by Nuclear Magnetic Resonance," *Science,* **171** (March 19, 1971): 1151-1153

This is what makes MRI useful!

Putting our Instrument to use

The confrontation with reality . . .

Revisit many other of yesterday's great discoveries . . .

that we neglected to think about!

Nature is a bitch!

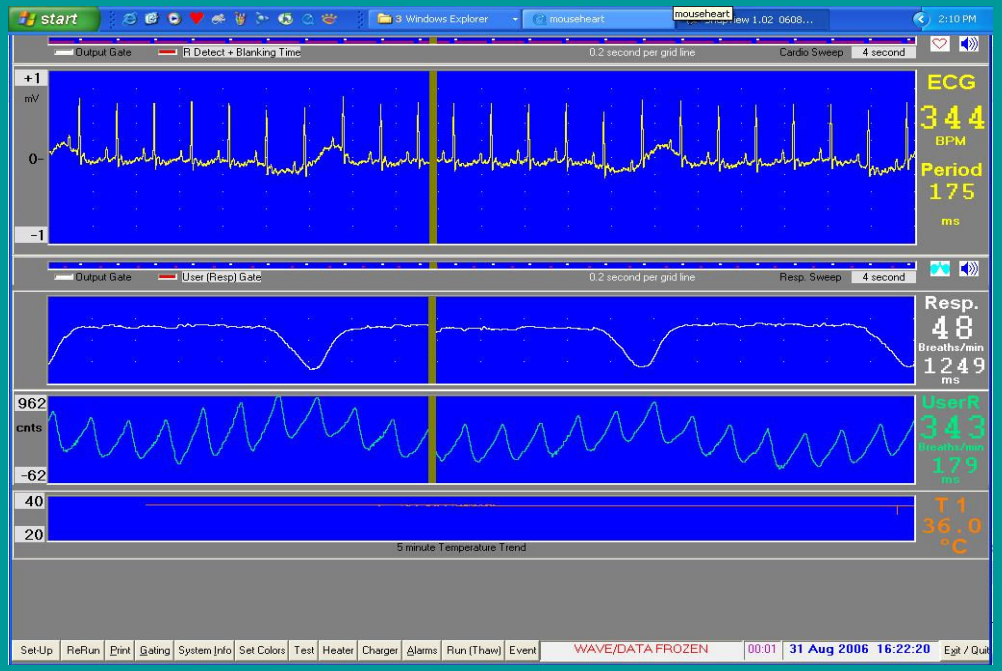
- We do not live in an ideal world.
- None of our simplifying assumptions are valid!
- How do we eliminate all the complicating effects?
- Well, its all Physics too!

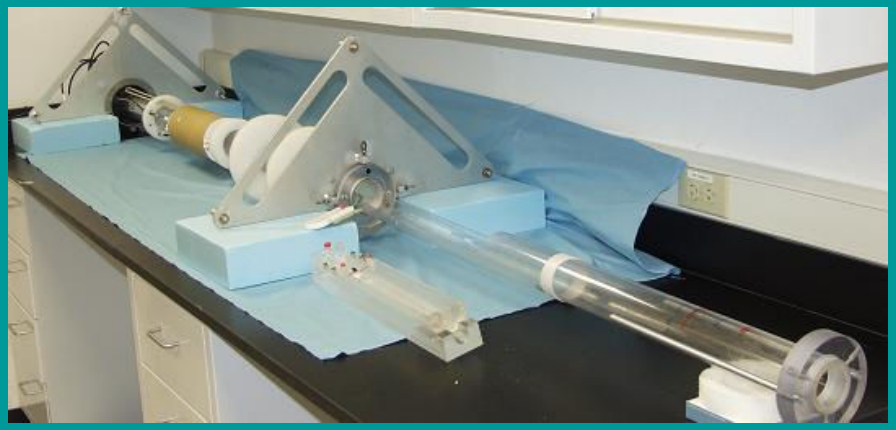
A few complaints:

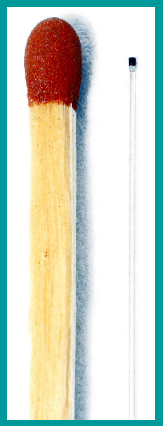
- The signal is too weak
- A uniform magnetic field is impossible
- Eddy Currents!! Who ordered that?
- Can’t you hold still????

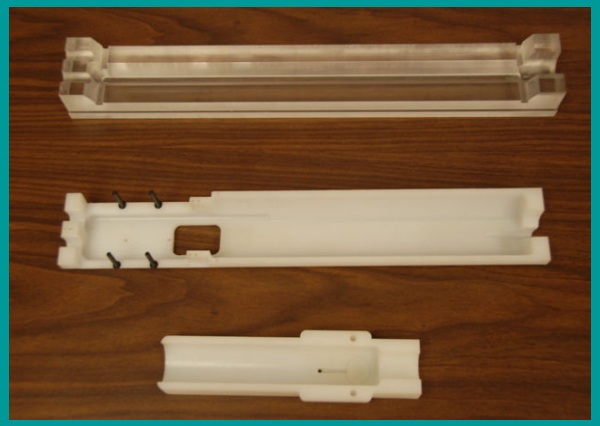
This is what makes instrumentation fun!

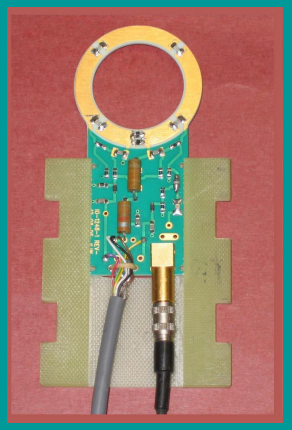
And leads to more instrumentation . . .







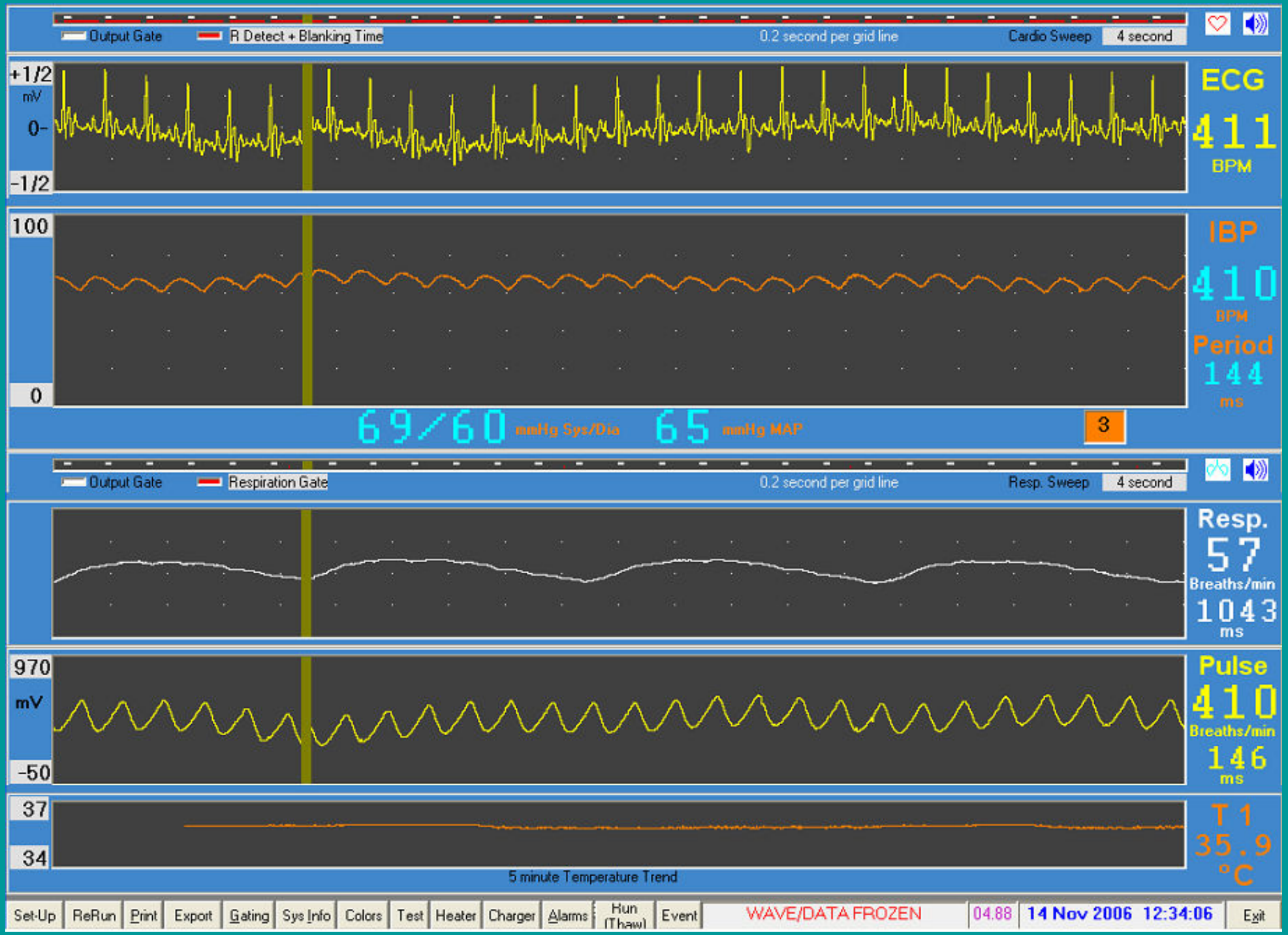




Physiologic Parameters of Interest

- ECG >600 beats/min
- Respiration >250 breaths/min
- Temperature 25 – 40 ^{o}C
- Blood pressure <300 mmHg
- Peripheral pulse waveform & heart rate
- Oxymetry waveform, heart rate & O_2 saturation
- Capnography waveform & end-tidal CO_2
- *Any suggestions ??*

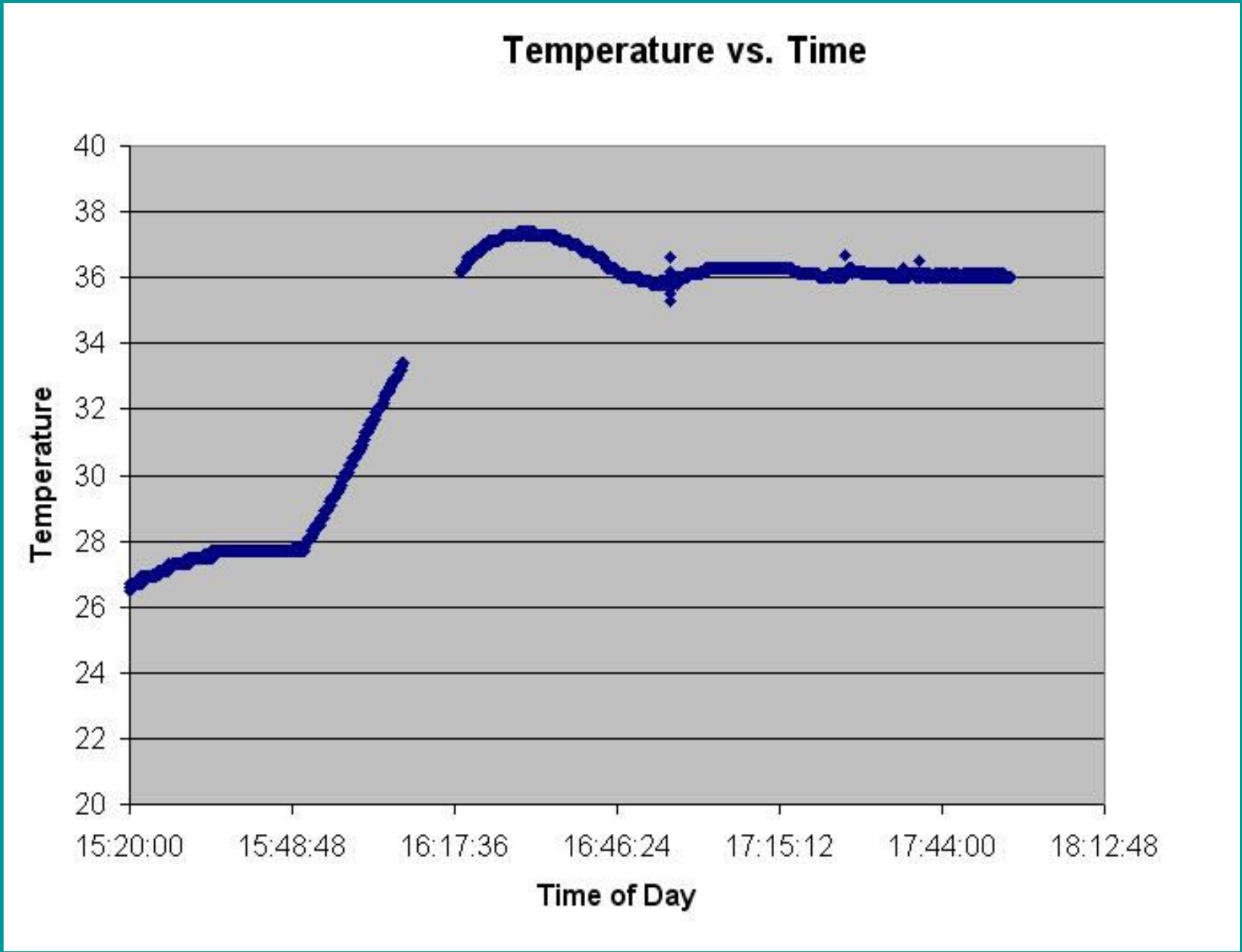
Inspiration/BP
Module
Control / Gating
Module
SAII

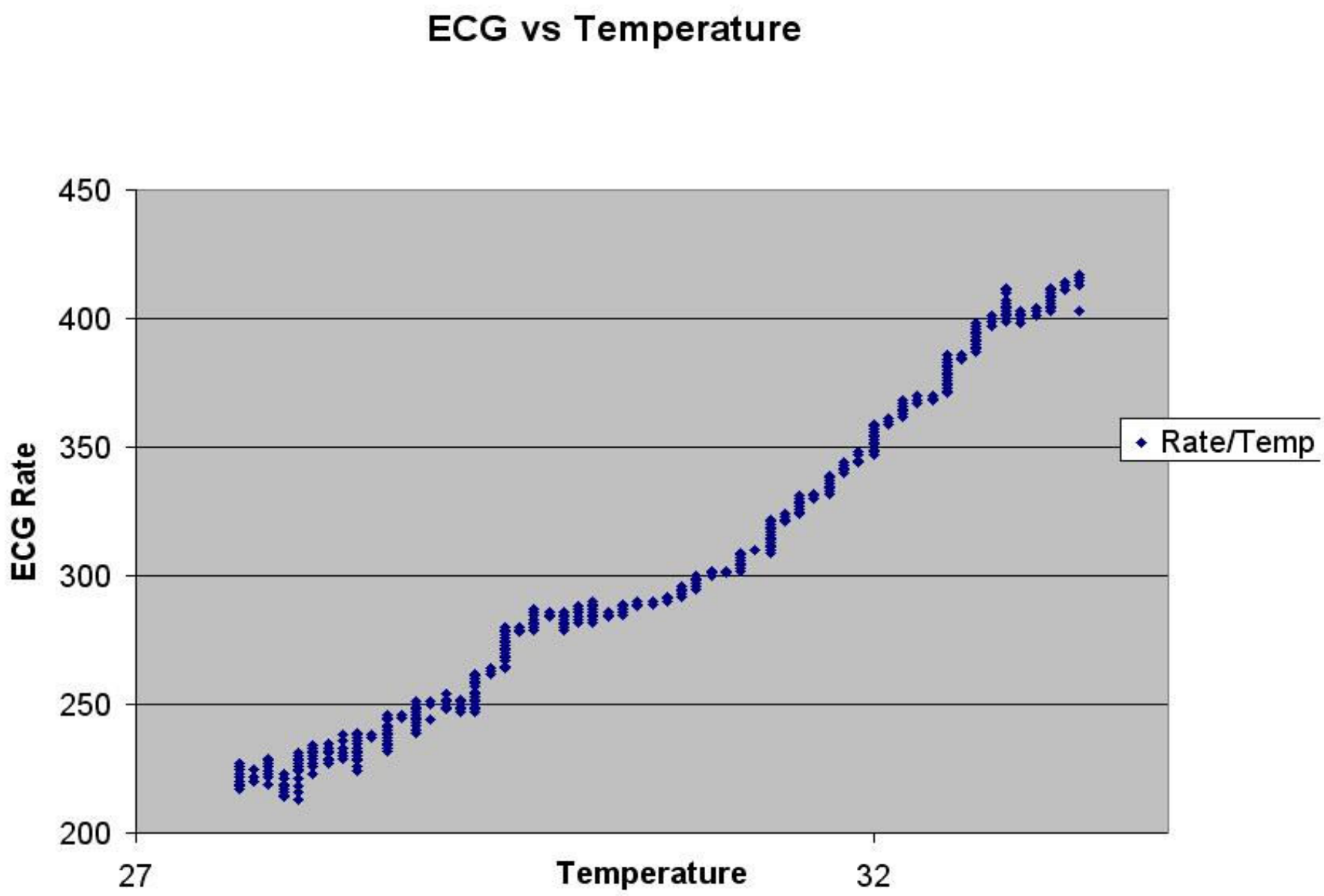

Output Gate
R Detect + Blanking Time
0.2 second per grid line
Cardio Sweep
4 second
+1/2
mV
0
-1/2
ECG
411
BPM
100
0
IBP
410
BPM
Period
144
ms
69/60 mmHg Sys/Dia
65 mmHg MAP
3
Output Gate
Respiration Gate
0.2 second per grid line
Resp. Sweep
4 second
Resp.
57
Breaths/min
1043
ms
970
mV
-50
Pulse
410
Breaths/min
146
ms
37
34
T 1
35.9
°C
5 minute Temperature Trend
Set-Up
ReRun
Print
Export
Gating
Sys Info
Colors
Test
Heater
Charger
Alarms
Run (Thaw)
Event
WAVE/DATA FROZEN
04.88
14 Nov 2006 12:34:06
Exit

What for?

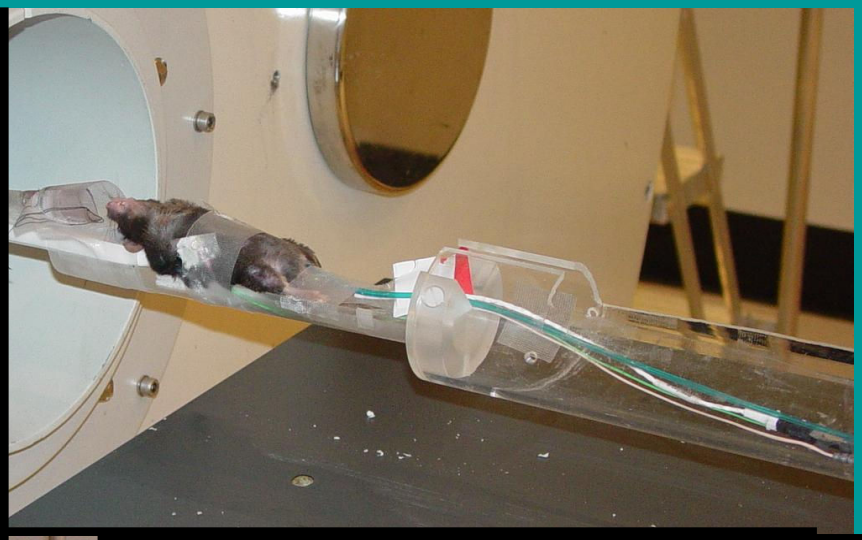
- Anesthesia maintenance & care of subject
- Detect response to stimulus or injection
- Control of Physiologic Parameters
- Synchronization of Image acquisition

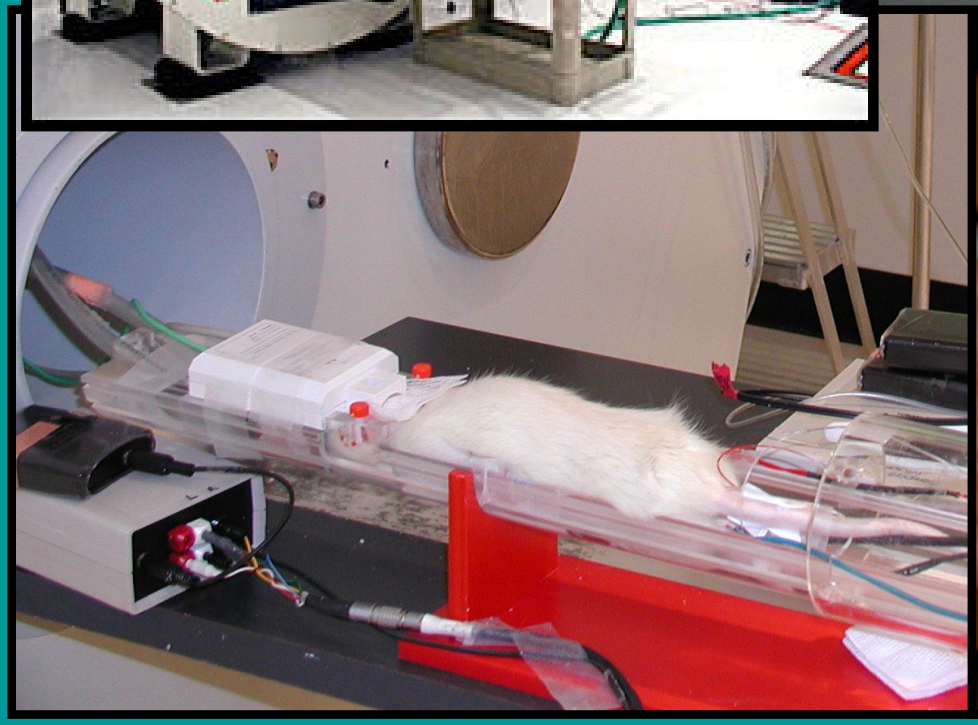
THIS SIDE UP
Heater
Module
MR-compatible
Small Animal Heating System
SA Instruments, Inc.
Fan
Module
MR-compatible
Small Animal Heating System
SA Instruments, Inc.

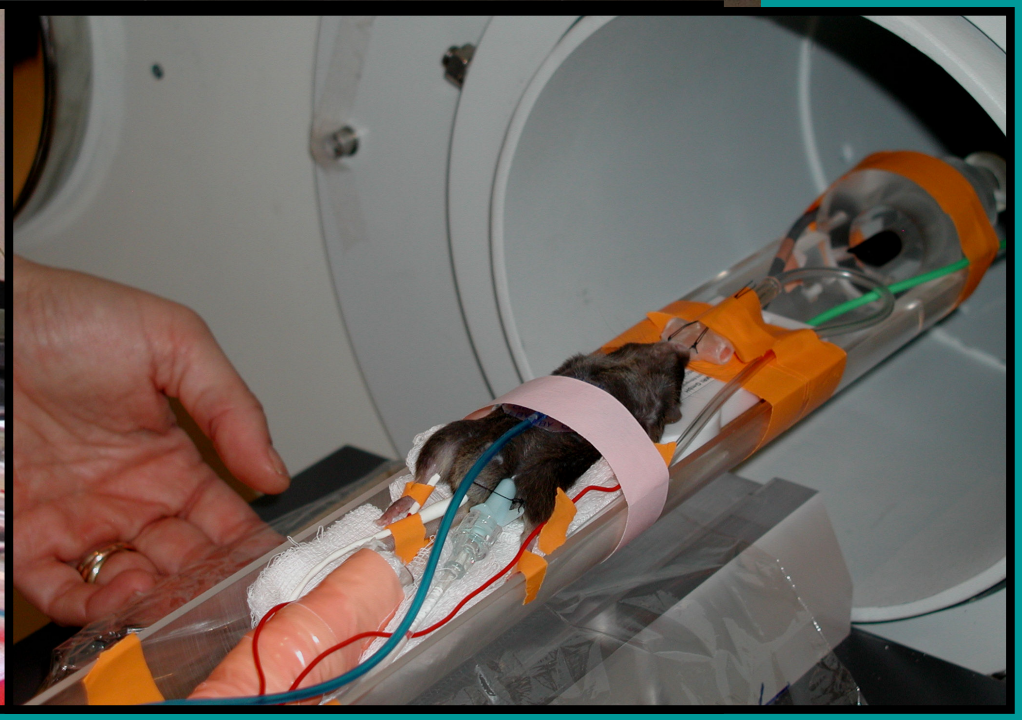

Temperature vs. Time
Temperature
40
38
36
34
32
30
28
26
24
22
20
15:20:00
15:48:48
16:17:36
16:46:24
17:15:12
17:44:00
18:12:48
Time of Day

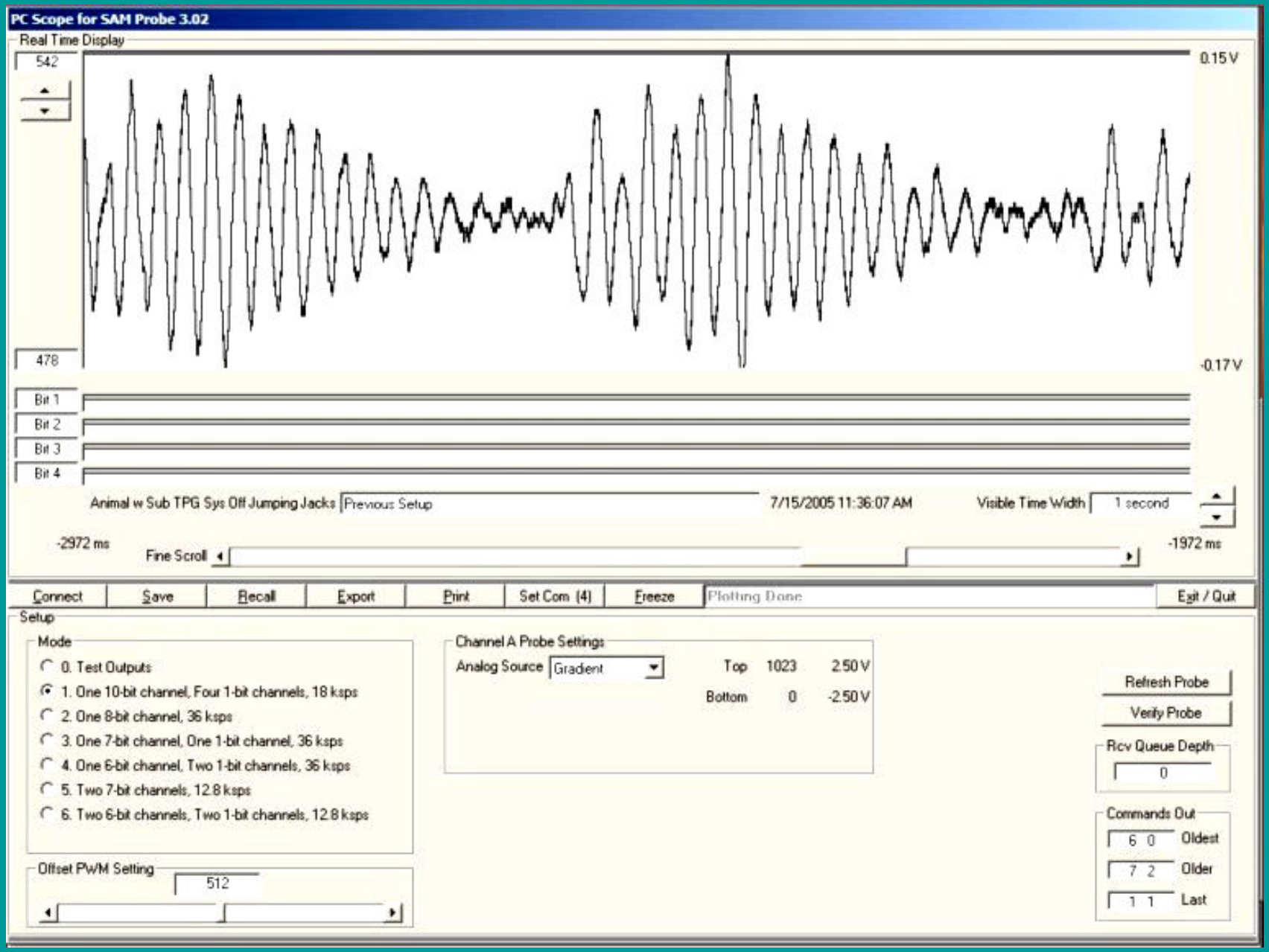

ECG vs Temperature
450
400
350
300
250
200
ECG Rate
27
Temperature
32
Rate/Temp

9.4T microMRI: Animal Positioning & monitoring

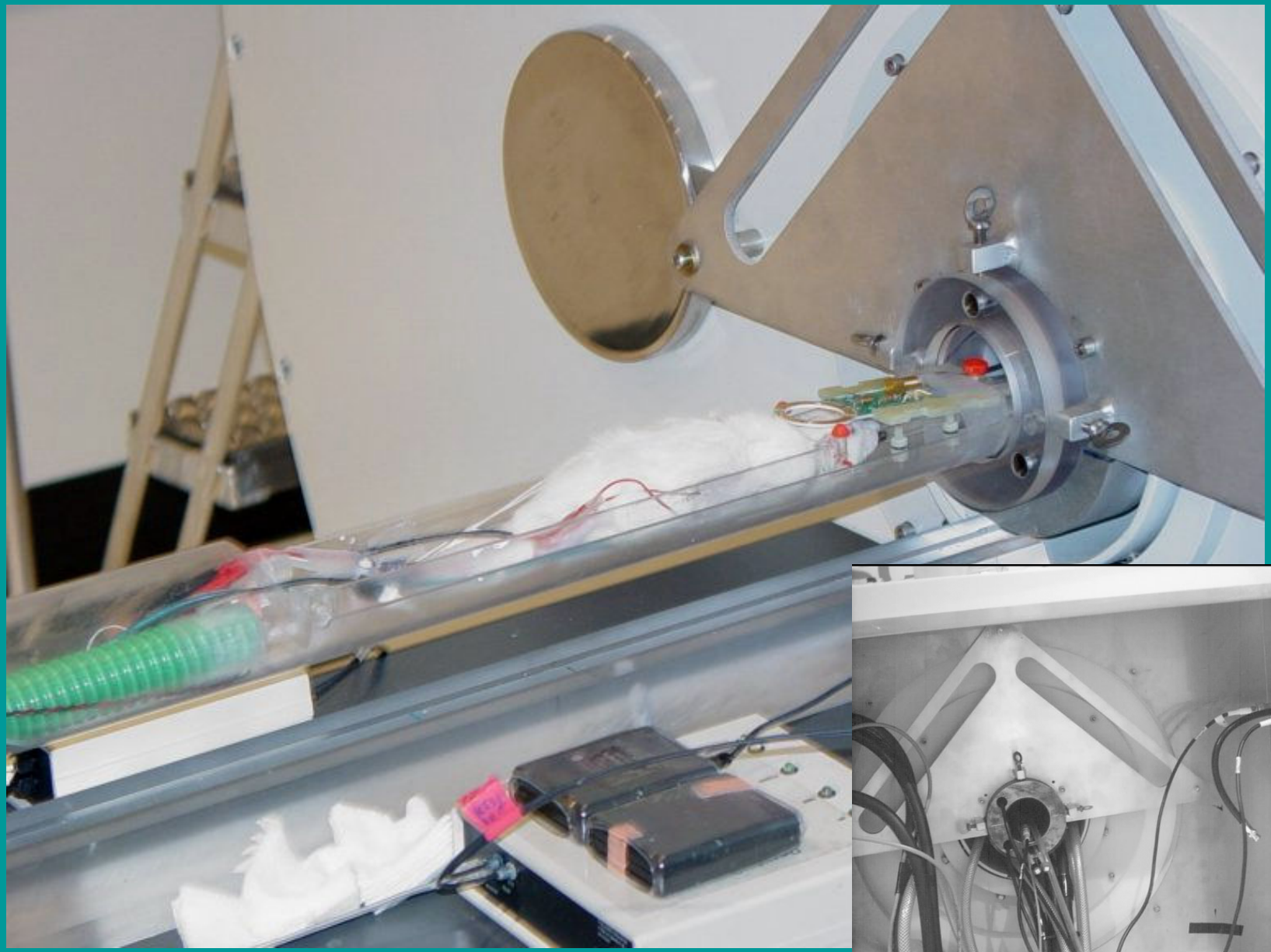




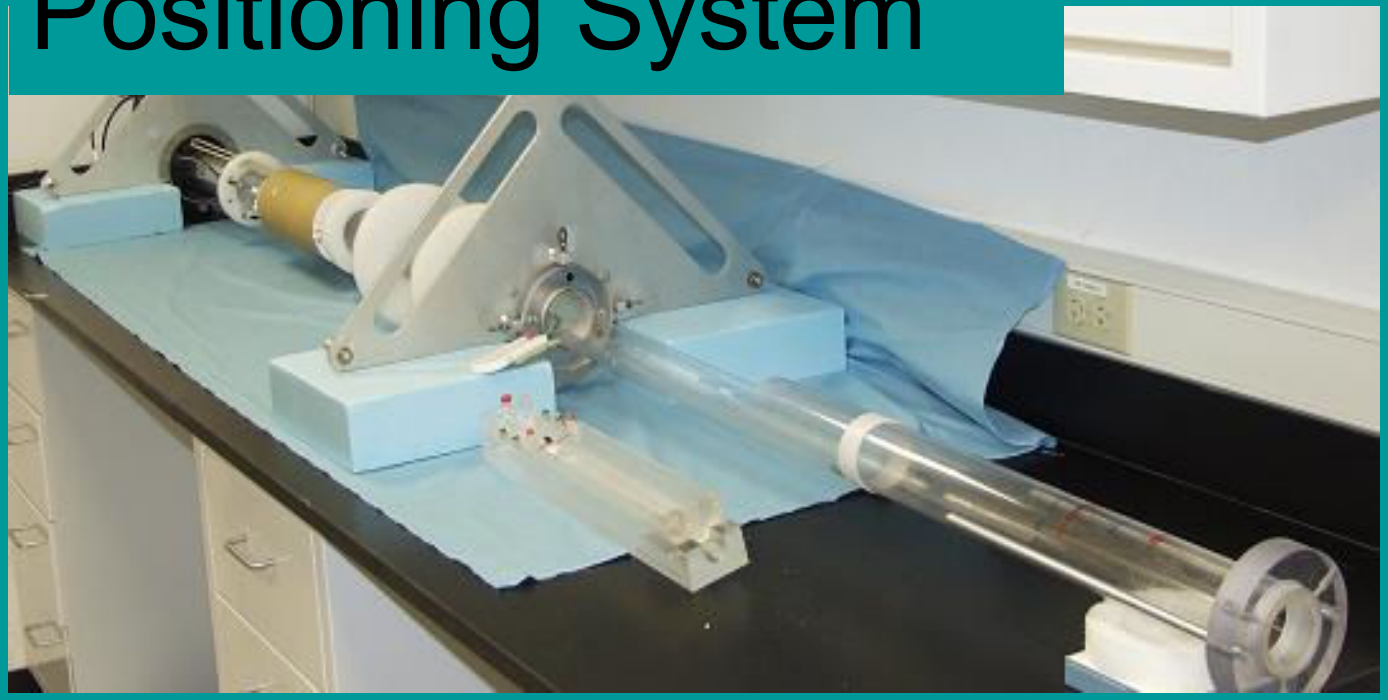


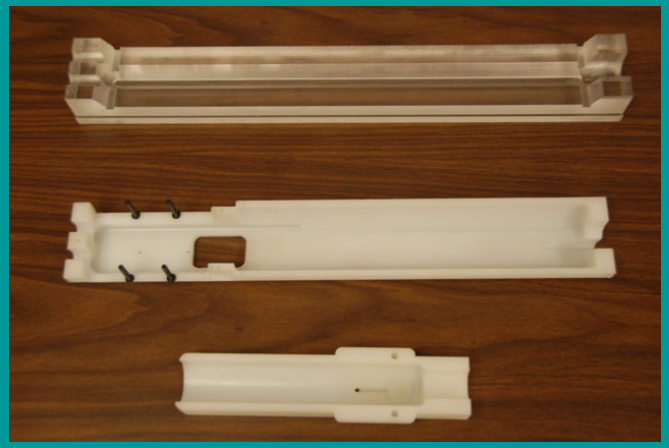

PC Scope for SAM Probe 3.02
Real Time Display
542
478
0.15 V
-0.17 V
Bit 1
Bit 2
Bit 3
Bit 4
Animal w Sub TPG Sys Off Jumping Jacks
Previous Setup
7/15/2005 11:36:07 AM
Visible Time Width
1 second
-2972 ms
Fine Scroll
-1972 ms
Connect
Save
Recall
Export
Print
Set Com (4)
Freeze
Plotting Done
Exit / Quit
Setup
Mode
0. Test Outputs
1. One 10-bit channel, Four 1-bit channels, 18 ksps
2. One 8-bit channel, 36 ksps
3. One 7-bit channel, One 1-bit channel, 36 ksps
4. One 6-bit channel, Two 1-bit channels, 36 ksps
5. Two 7-bit channels, 12.8 ksps
6. Two 6-bit channels, Two 1-bit channels, 12.8 ksps
Offset PWM Setting
512
Channel A Probe Settings
Analog Source
Gradient
Top 1023 2.50 V
Bottom 0 -2.50 V
Refresh Probe
Verify Probe
Rcv Queue Depth
0
Commands Out
6 0 Oldest
7 2 Older
1 1 Last

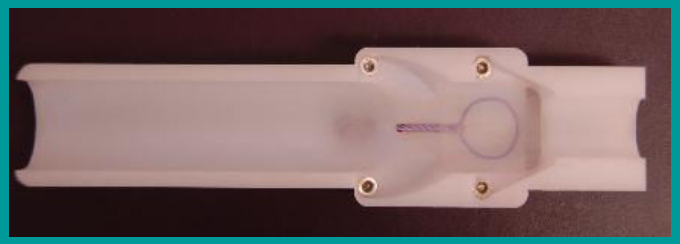
New Positioning System

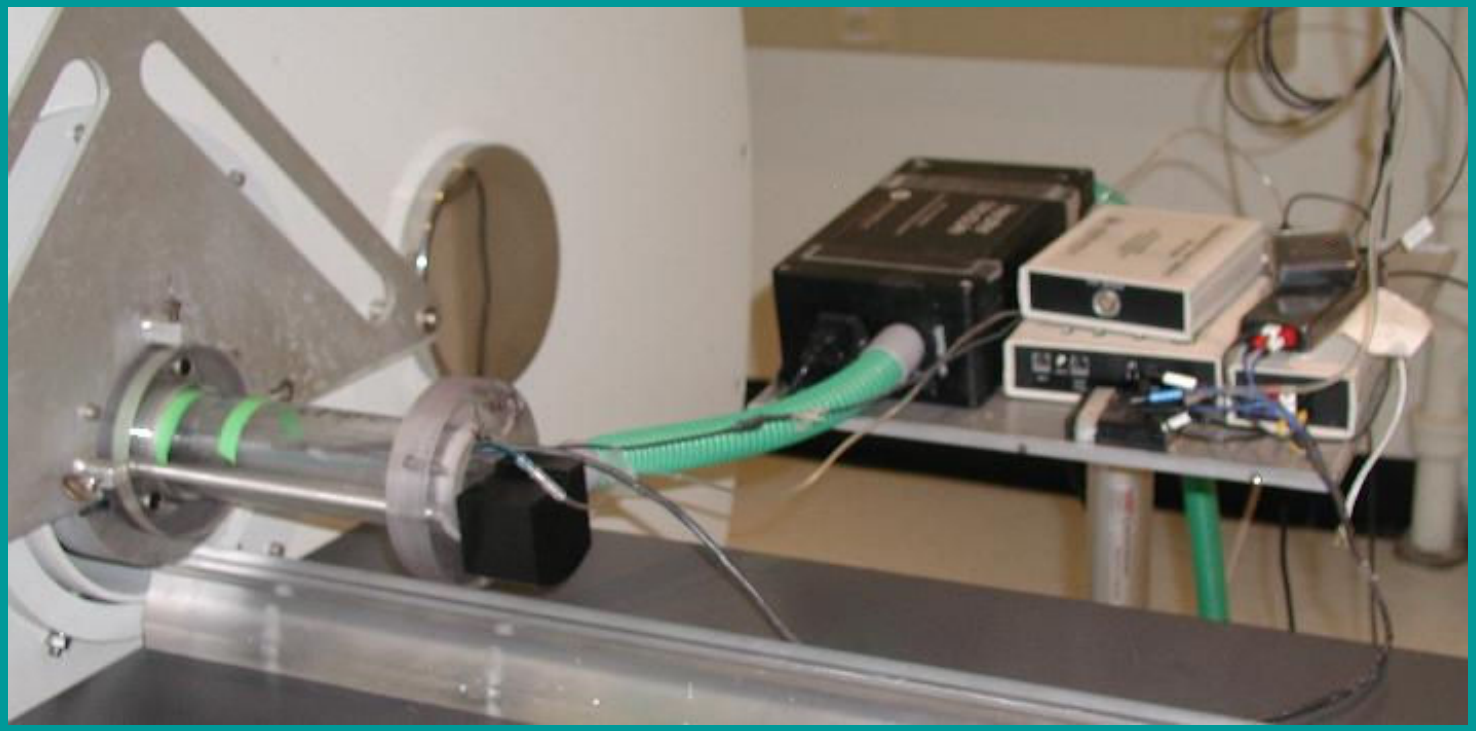


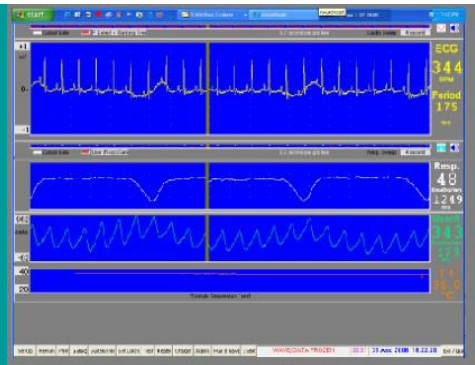
Positioning System

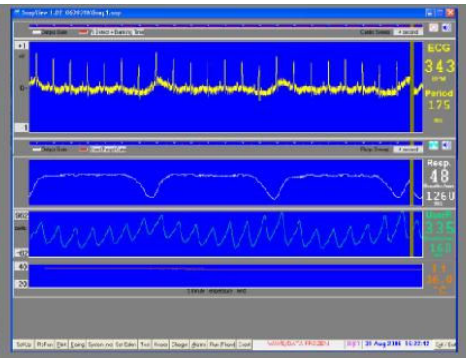




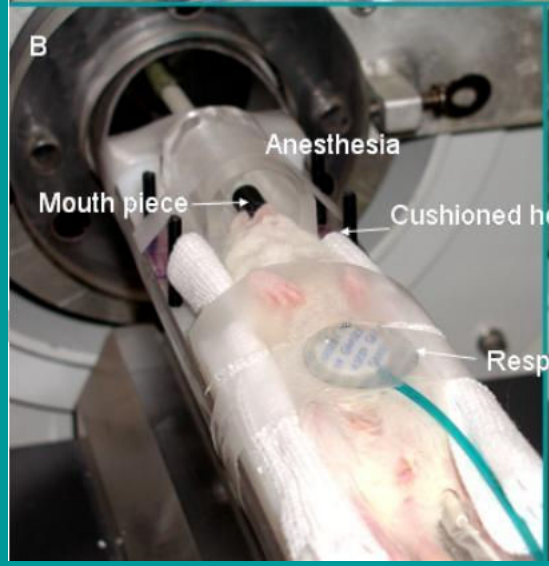


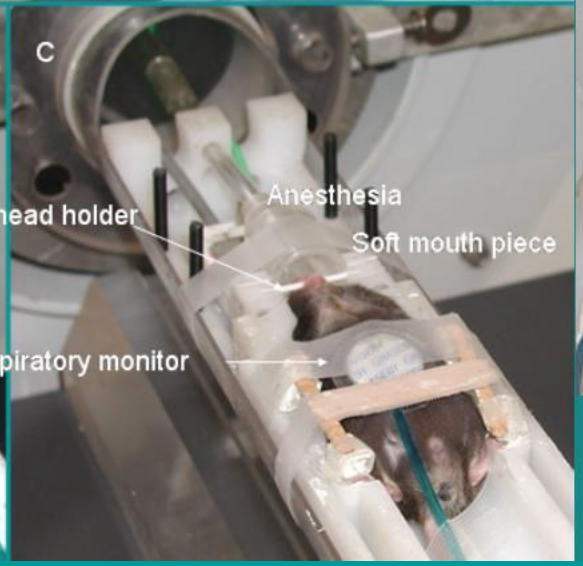


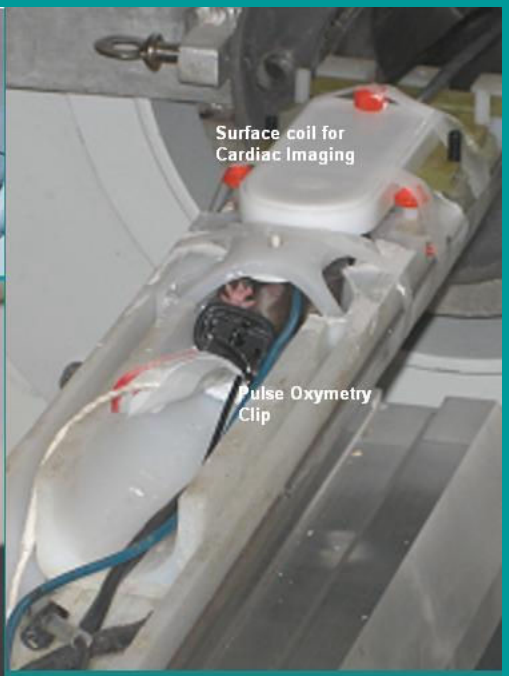




BROOKHAVEN
NATIONAL LABORATORY



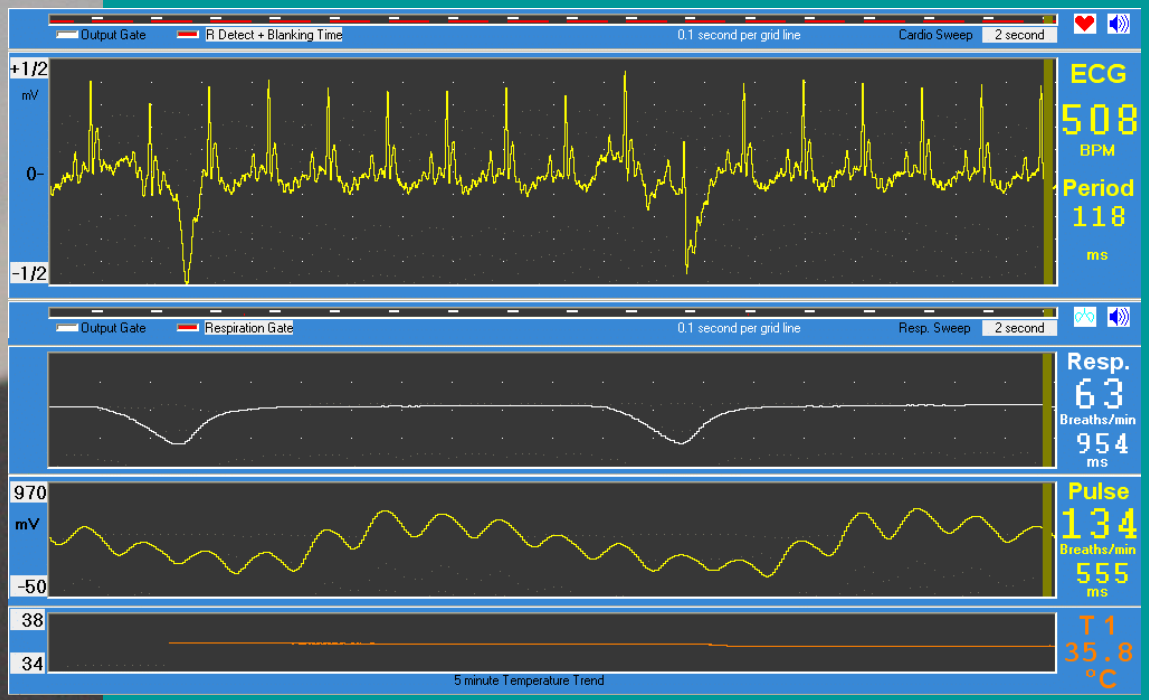




A variety of coil configurations are shown for different animals and regions of interest. Precise localization of the target anatomy within the magnetic field and with respect to all coil systems makes consistant imaging performance possible.

Mouse imaging

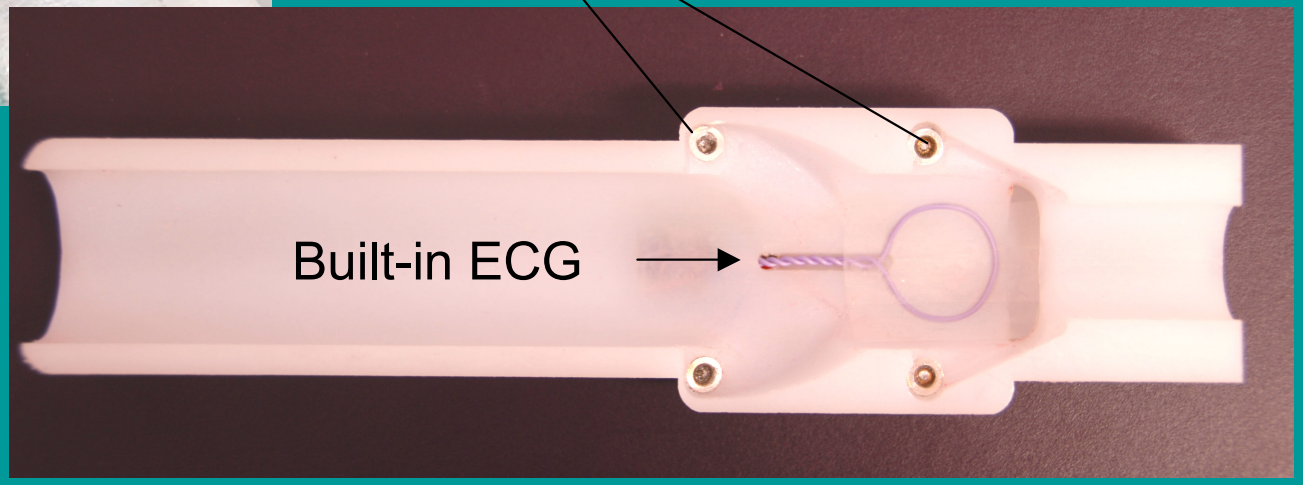
Mouseholder

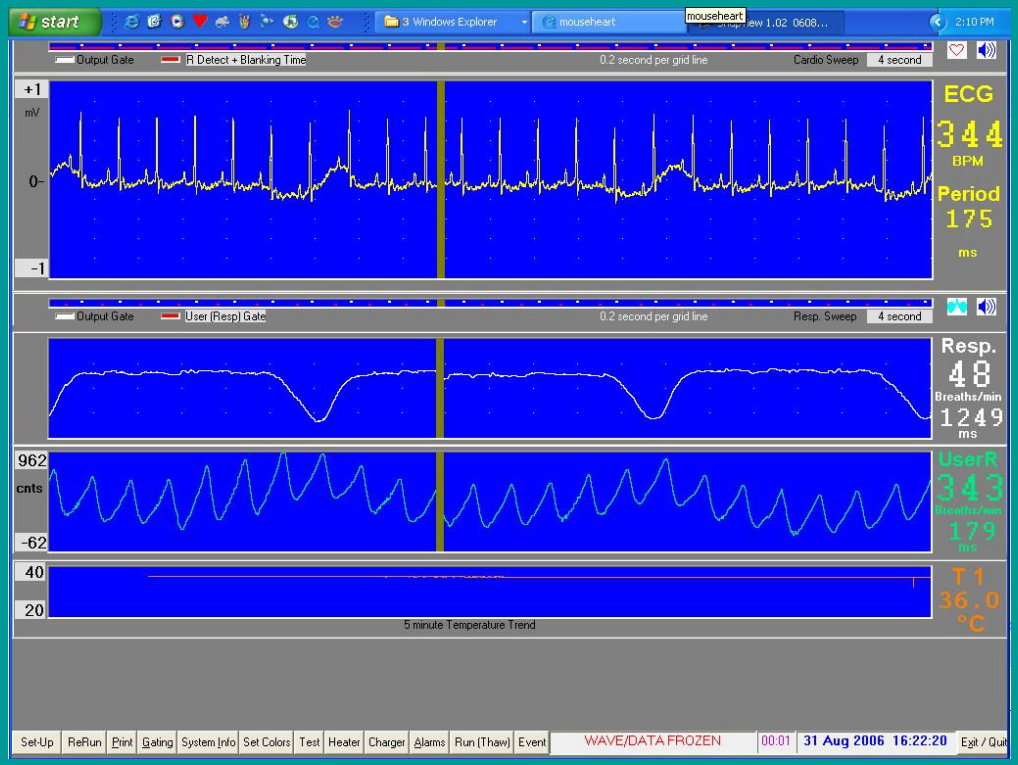


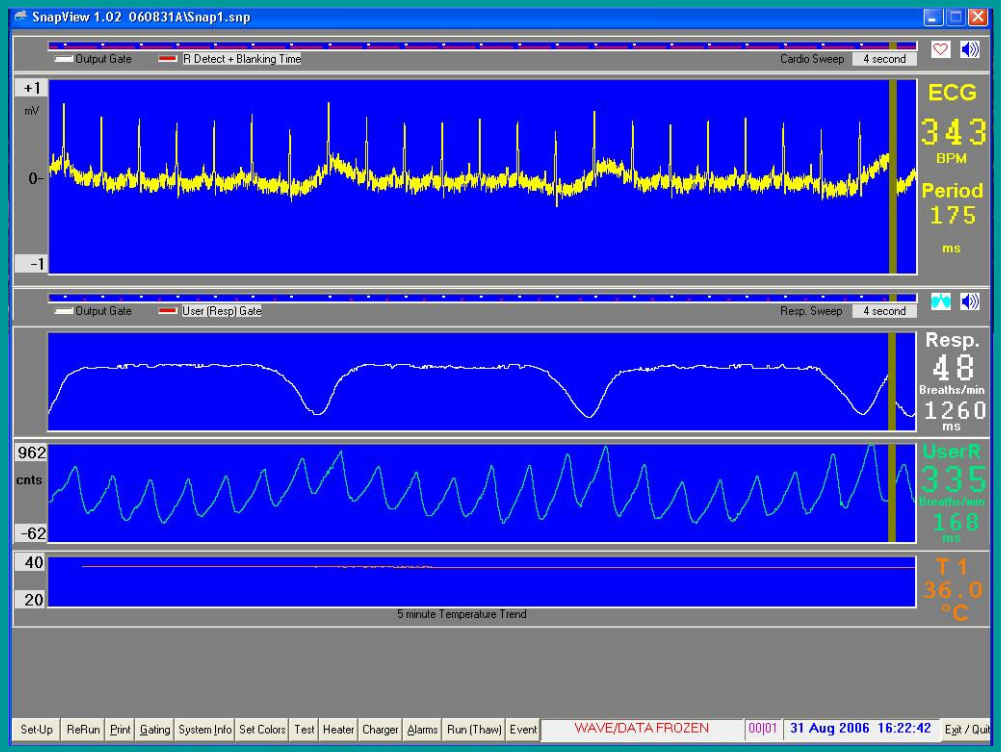
Respiratory frequency

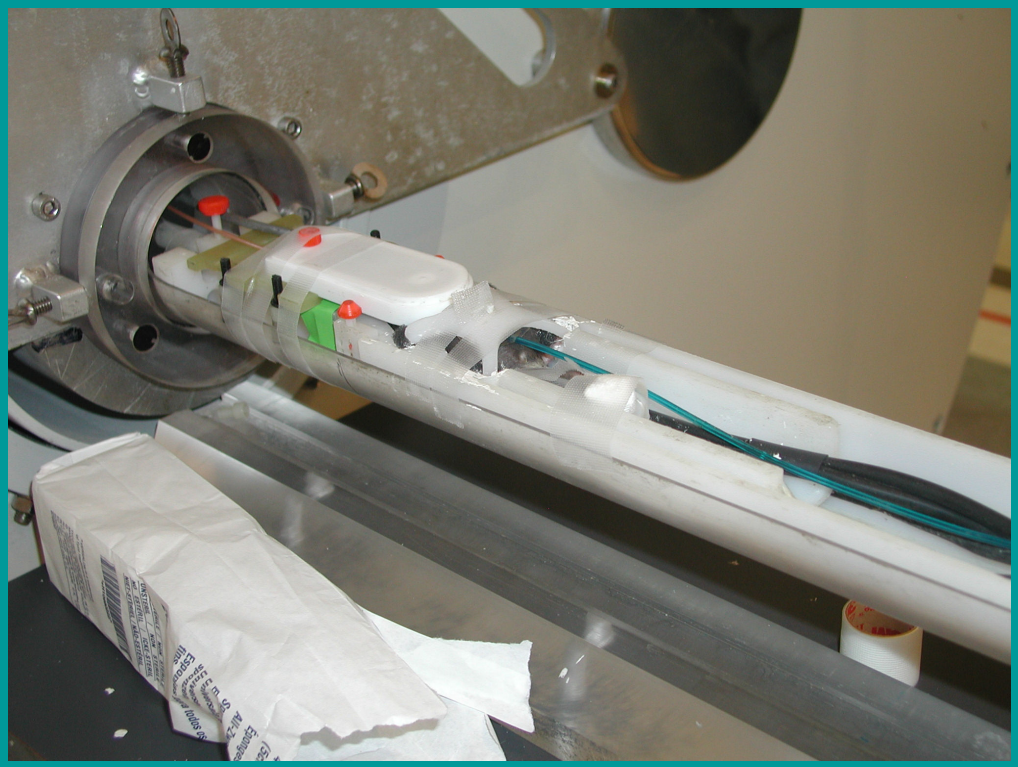
ECG-monitoring

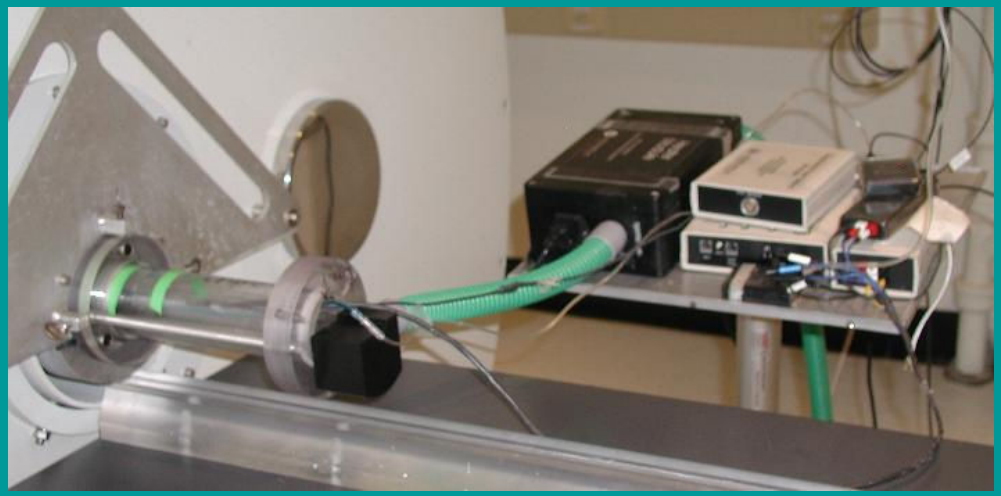
Pulse-(oximetry)…



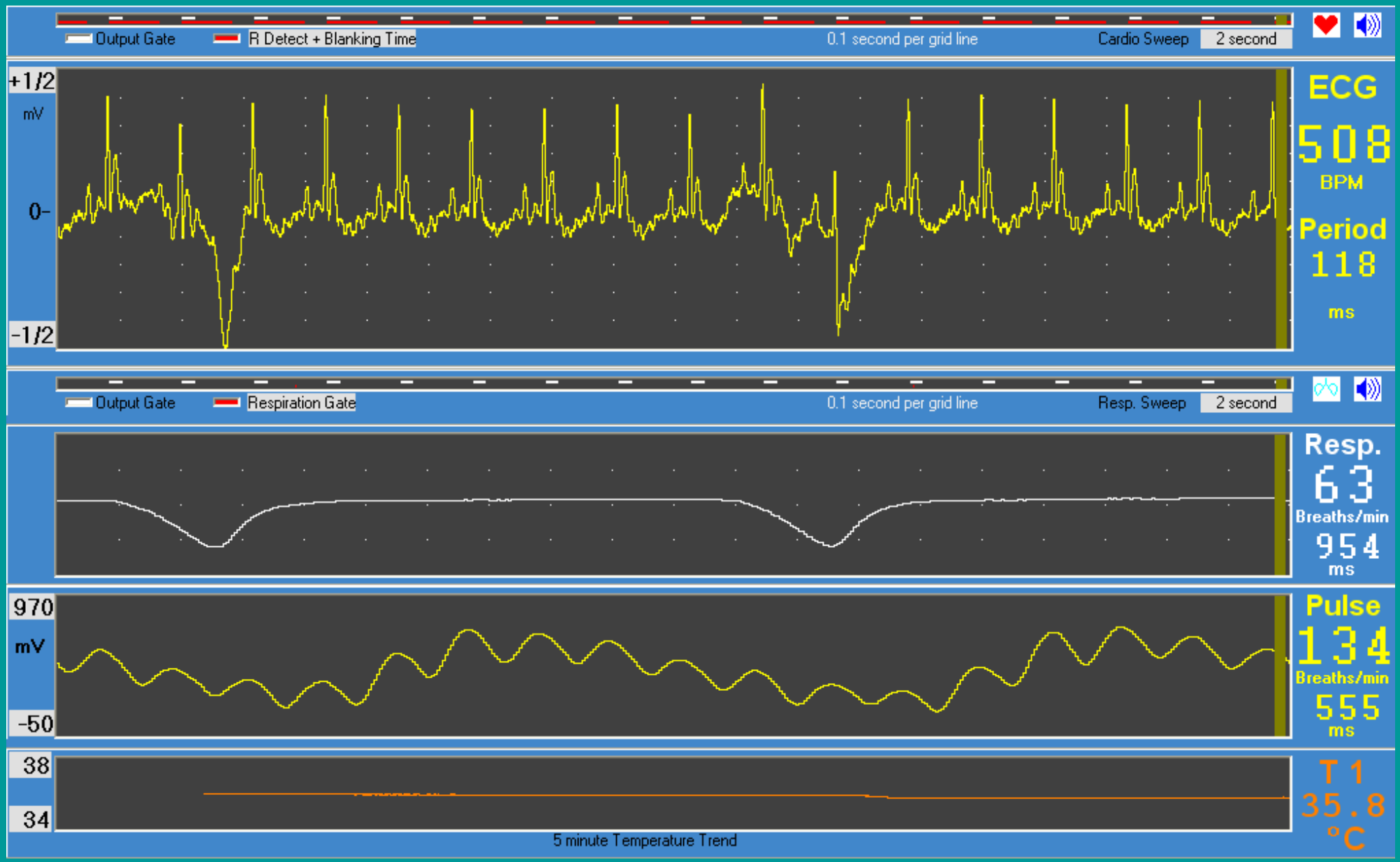

start
mouseheart
Output Gate
R Detect + Blanking Time
0.2 second per grid line
Cardio Sweep
4 second
+1
mV
0
-1
ECG
344
BPM
Period
175
ms
Output Gate
User (Resp) Gate
0.2 second per grid line
Resp. Sweep
4 second
Resp.
48
Breaths/min
1249
ms
962
cnts
-62
UserR
343
Breaths/min
179
ms
40
20
T 1
36.0
°C
5 minute Temperature Trend
Set-Up
ReRun
Print
Gating
System Info
Set Colors
Test
Heater
Charger
Alarms
Run (Thaw)
Event
WAVE/DATA FROZEN
00:01
31 Aug 2006 16:22:20
Exit / Quit


SnapView 1.02 060831A\Snap1.snp
Output Gate
R Detect + Blanking Time
Cardio Sweep
4 second
+1
mV
0
-1
ECG
343
BPM
Period
175
ms
Output Gate
User (Resp) Gate
Resp. Sweep
4 second
Resp.
48
Breaths/min
1260
ms
962
cnts
-62
UserR
335
Breaths/min
168
ms
40
20
T 1
36.0
°C
5 minute Temperature Trend
Set-Up
ReRun
Print
Gating
System Info
Set Colors
Test
Heater
Charger
Alarms
Run (Thaw)
Event
WAVE/DATA FROZEN
00:01
31 Aug 2006 16:22:42
Exit / Quit

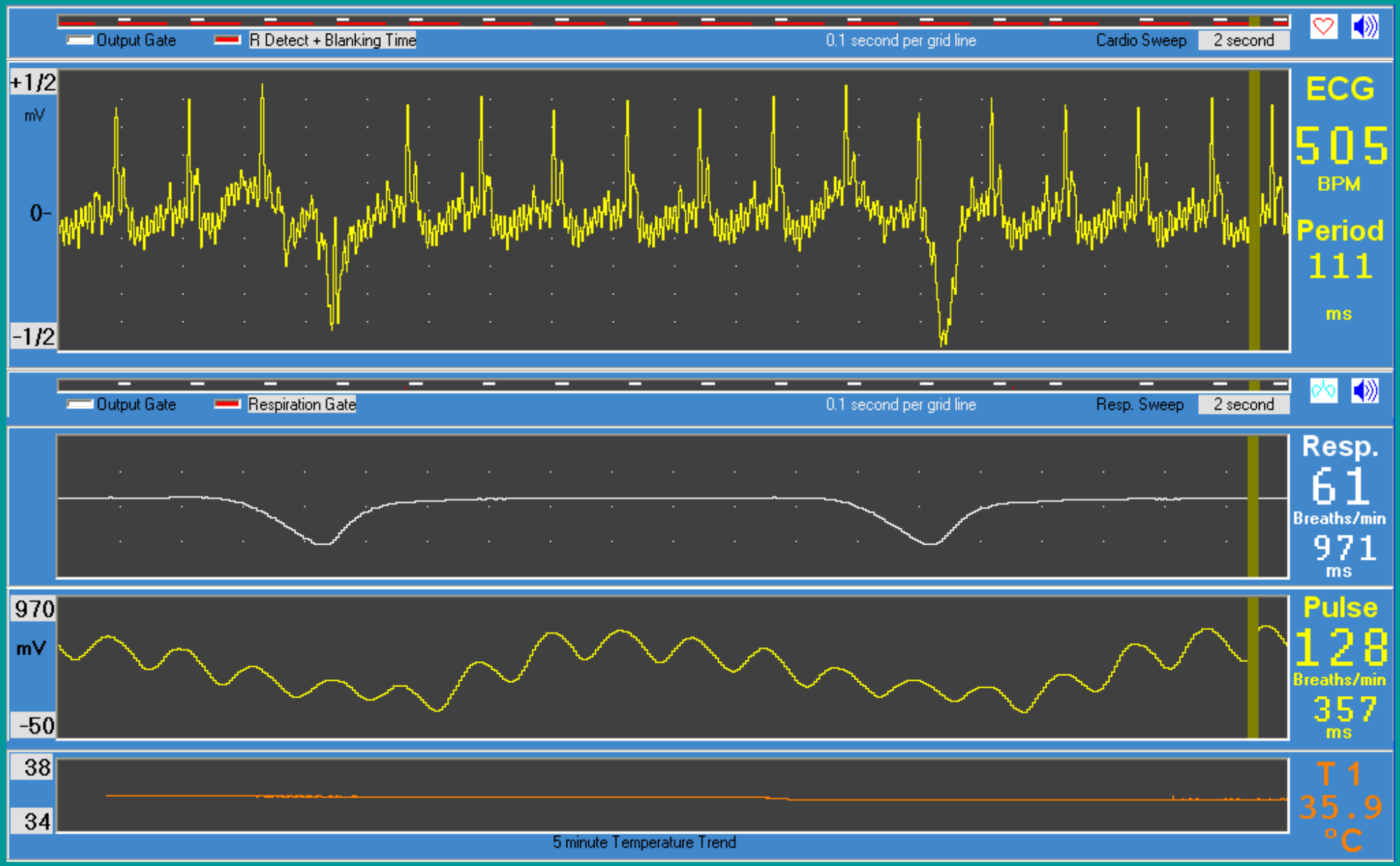


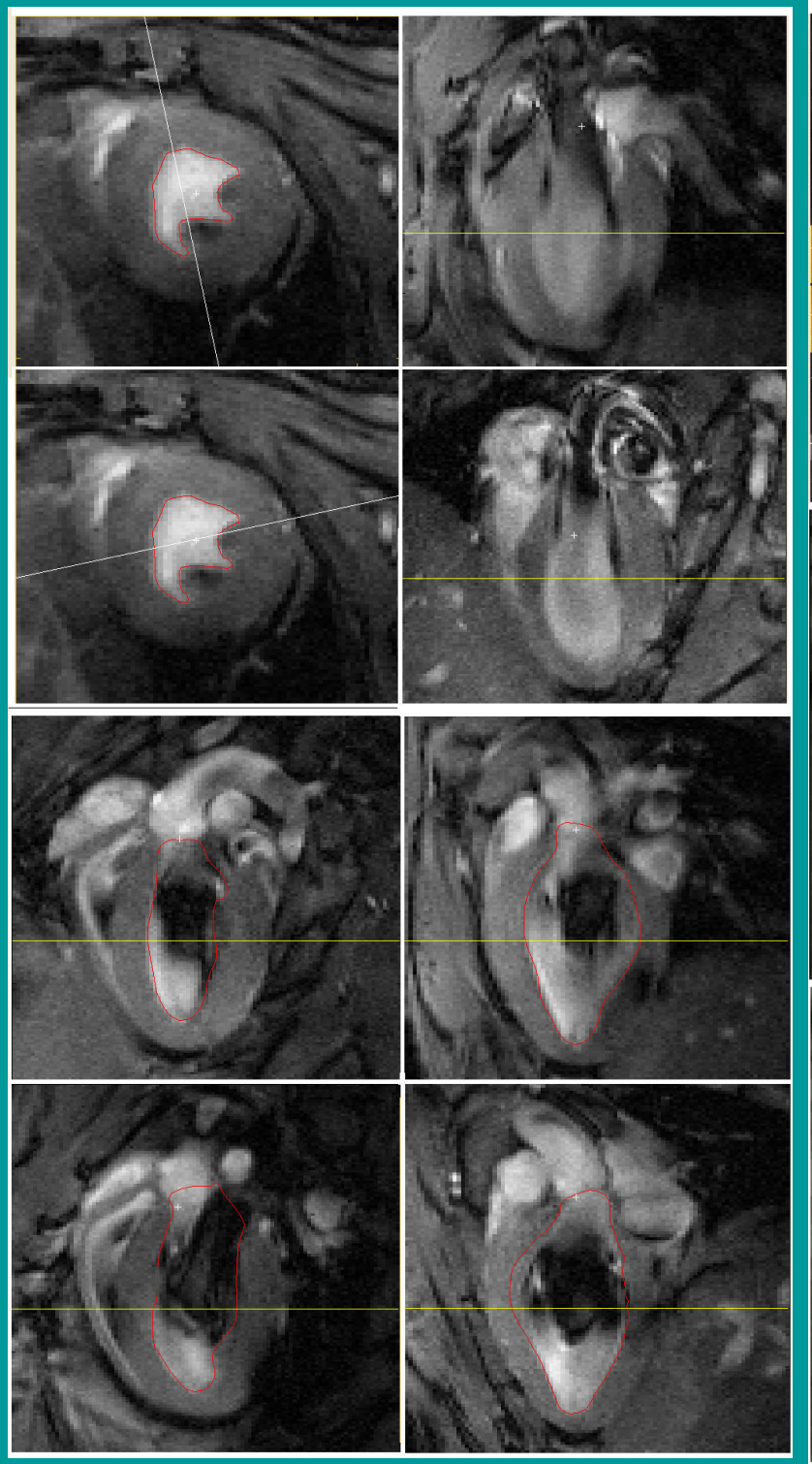


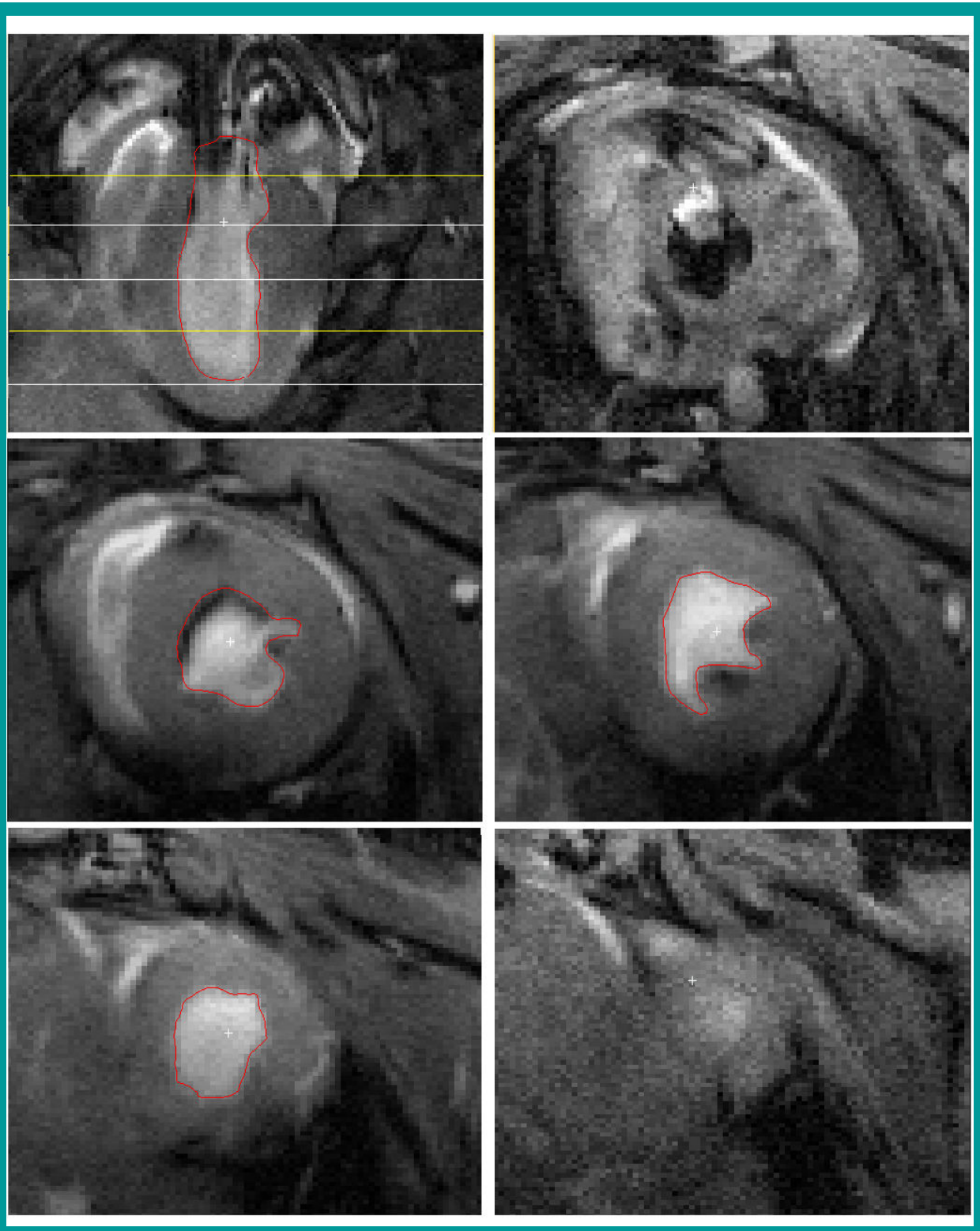
ECG system idle

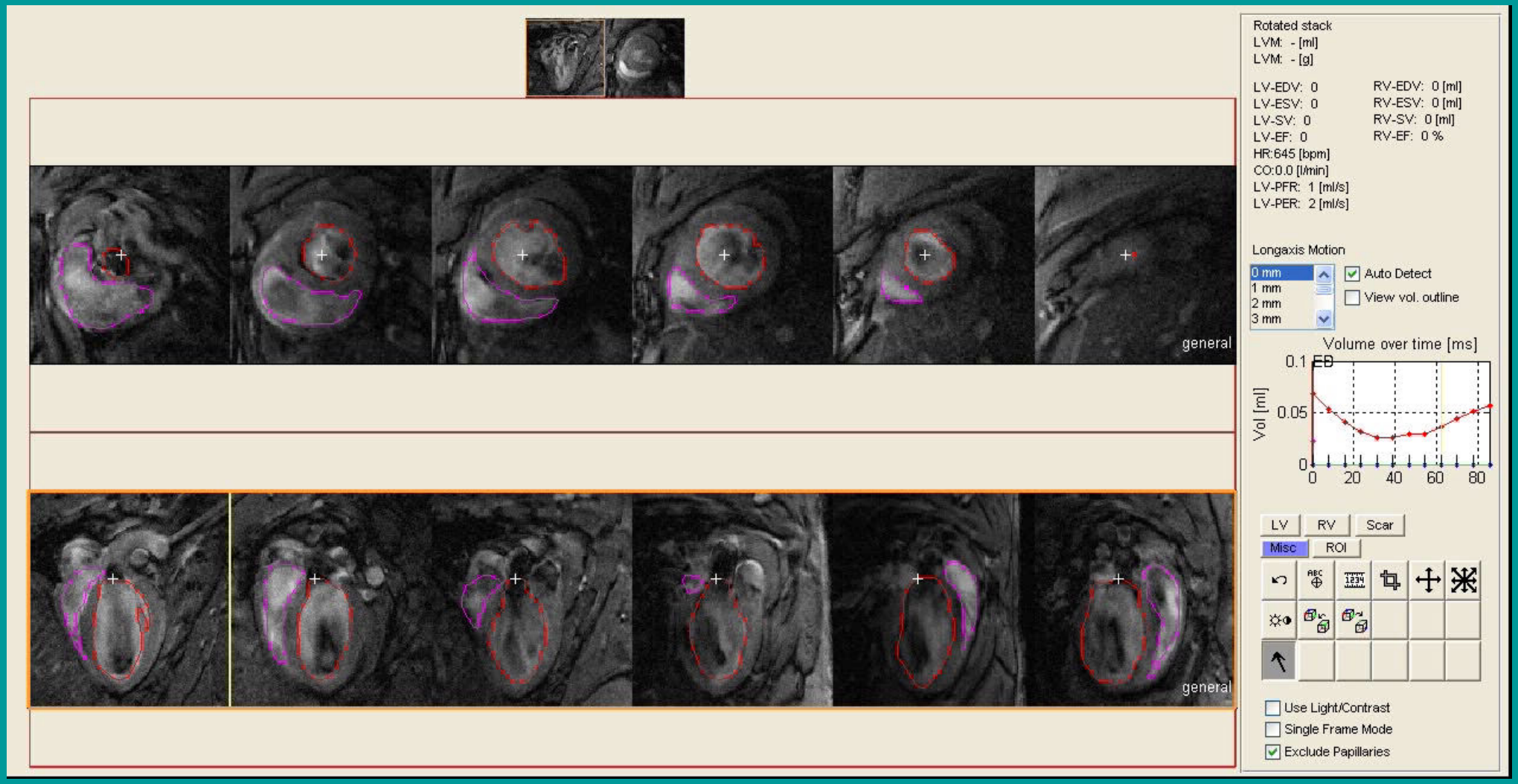


ECG system running









SEGMENT Software

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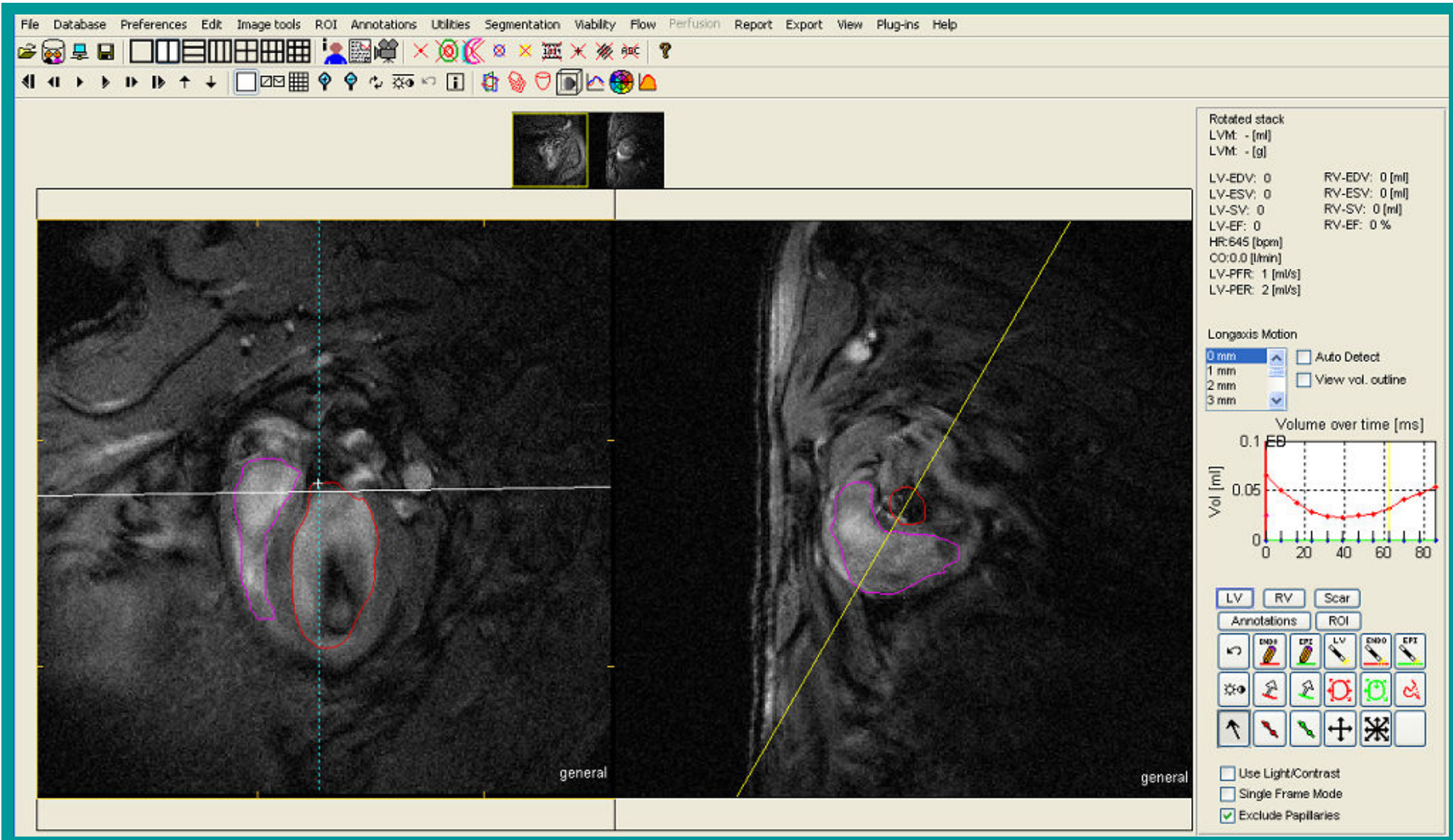
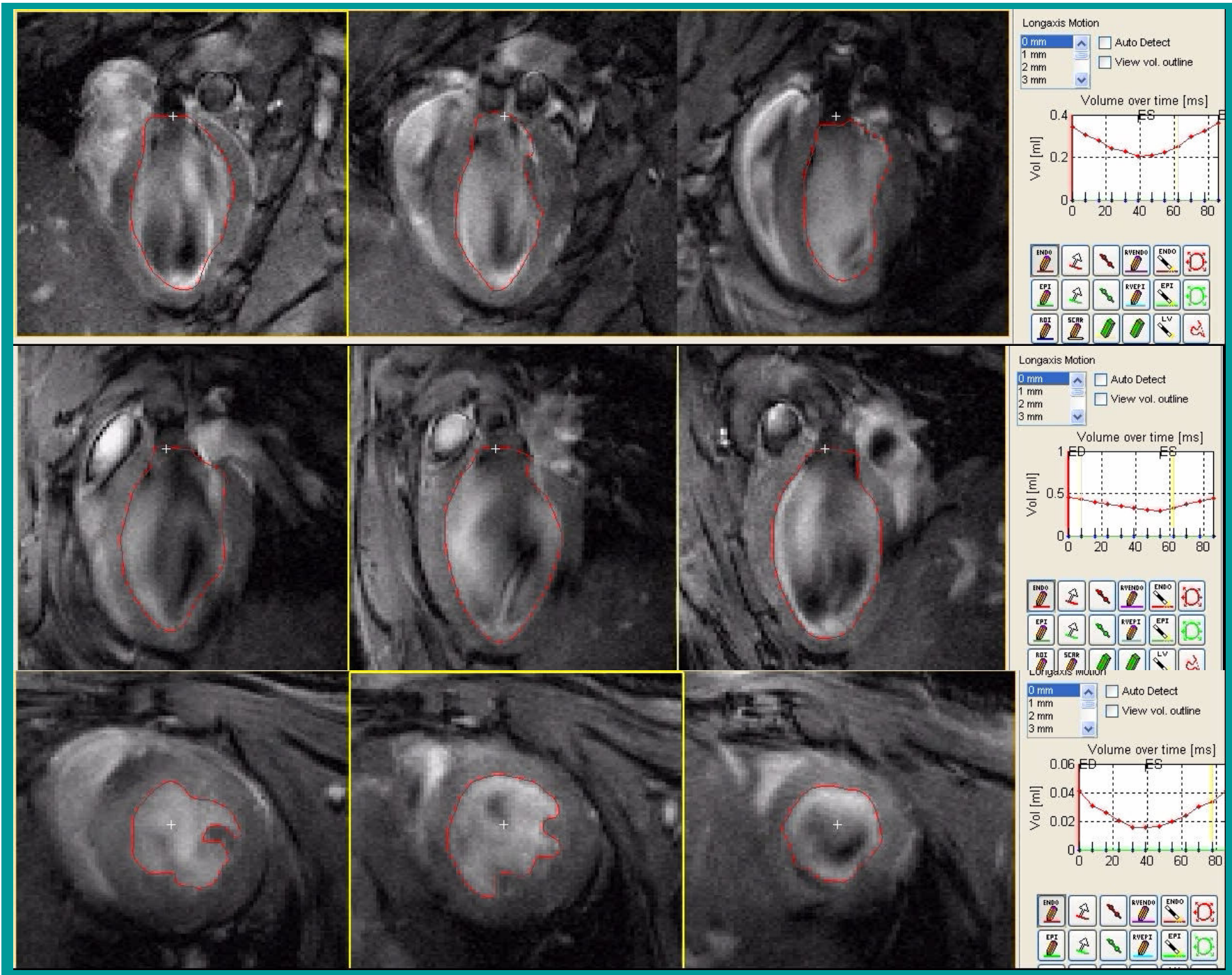
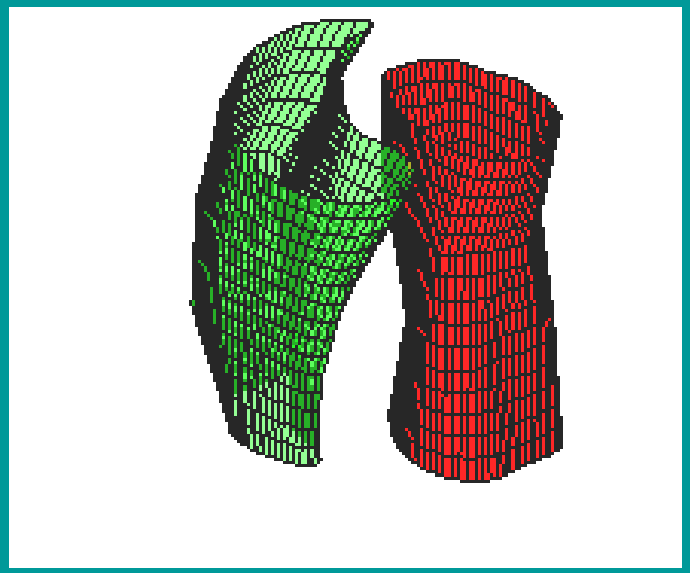
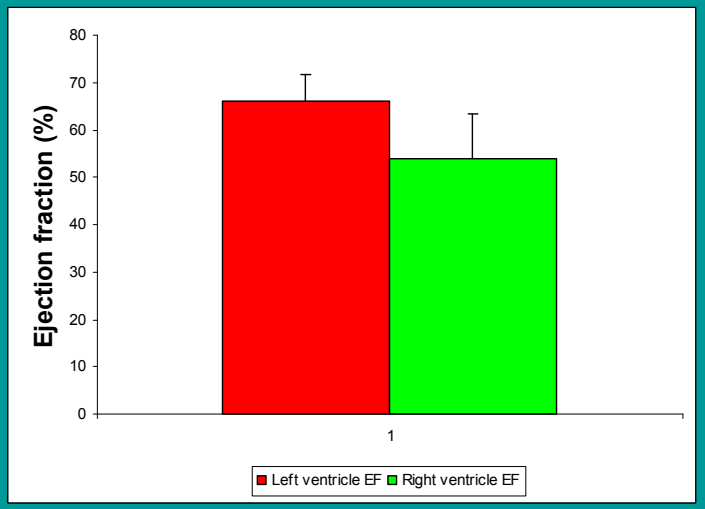
Version 1.682


File Database Preferences Edit Image tools ROI Annotations Utilities Segmentation Viability Flow Perfusion Report Export View Plug-ins Help
Rotated stack
LVM: - [ml]
LVM: - [g]
LV-EDV: 0
LV-ESV: 0
LV-SV: 0
LV-EF: 0
HR:645 [bpm]
CO:0.0 [l/min]
LV-PFR: 1 [ml/s]
LV-PER: 2 [ml/s]
RV-EDV: 0 [ml]
RV-ESV: 0 [ml]
RV-SV: 0 [ml]
RV-EF: 0 %
Longaxis Motion
0 mm
1 mm
2 mm
3 mm
Auto Detect
View vol. outline
Volume over time [ms]
Vol [ml]
0.1
0.05
0
ED
0
20
40
60
80
LV
RV
Scar
Annotations
ROI
Use Light/Contrast
Single Frame Mode
Exclude Papillaries
general
general

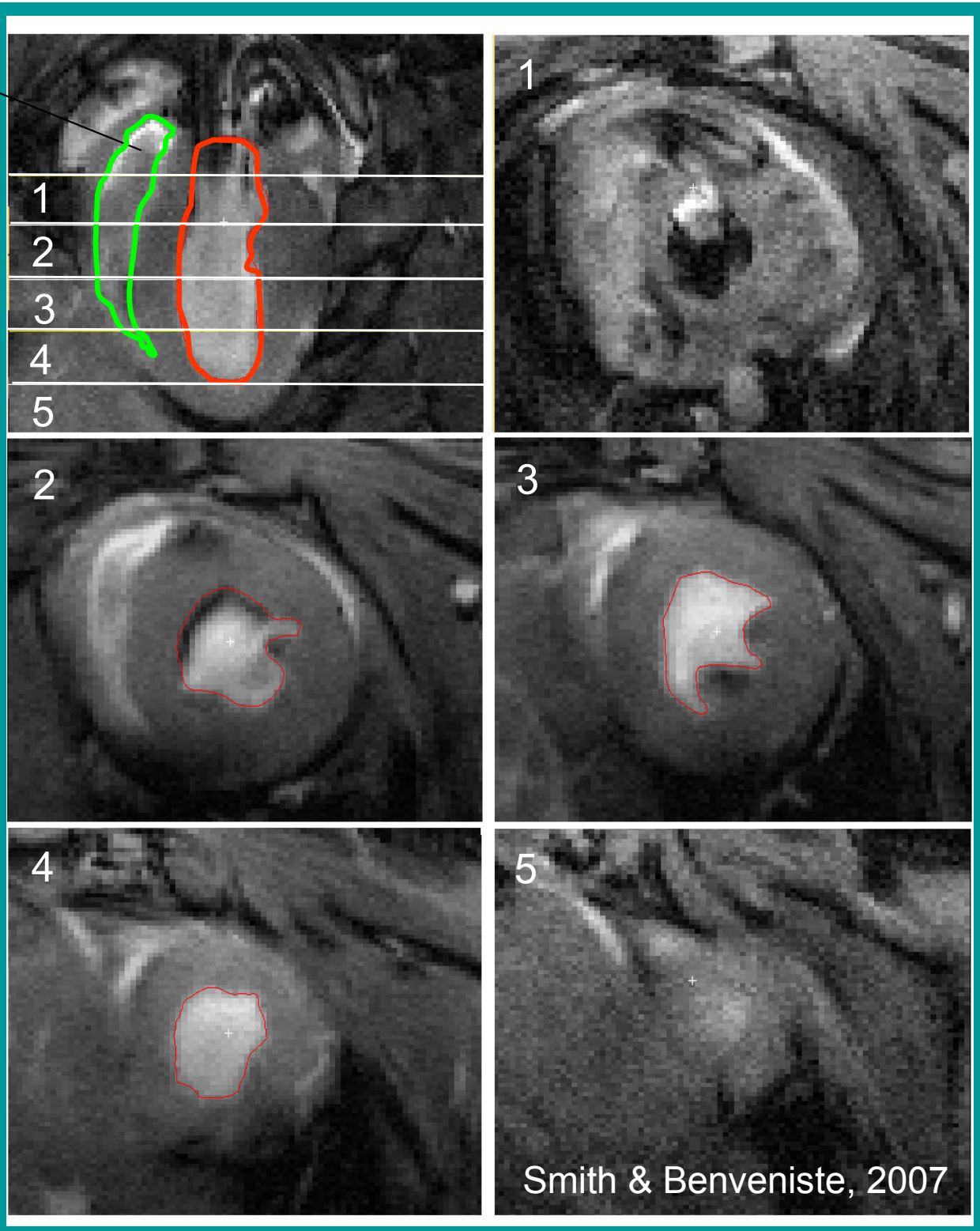

Longaxis Motion
0 mm
1 mm
2 mm
3 mm
Auto Detect
View vol. outline
Volume over time [ms]
Vol [ml]
ED
ES
ENDO
RVENDO
EPI
RVEPI
ROI
SCAR
LV

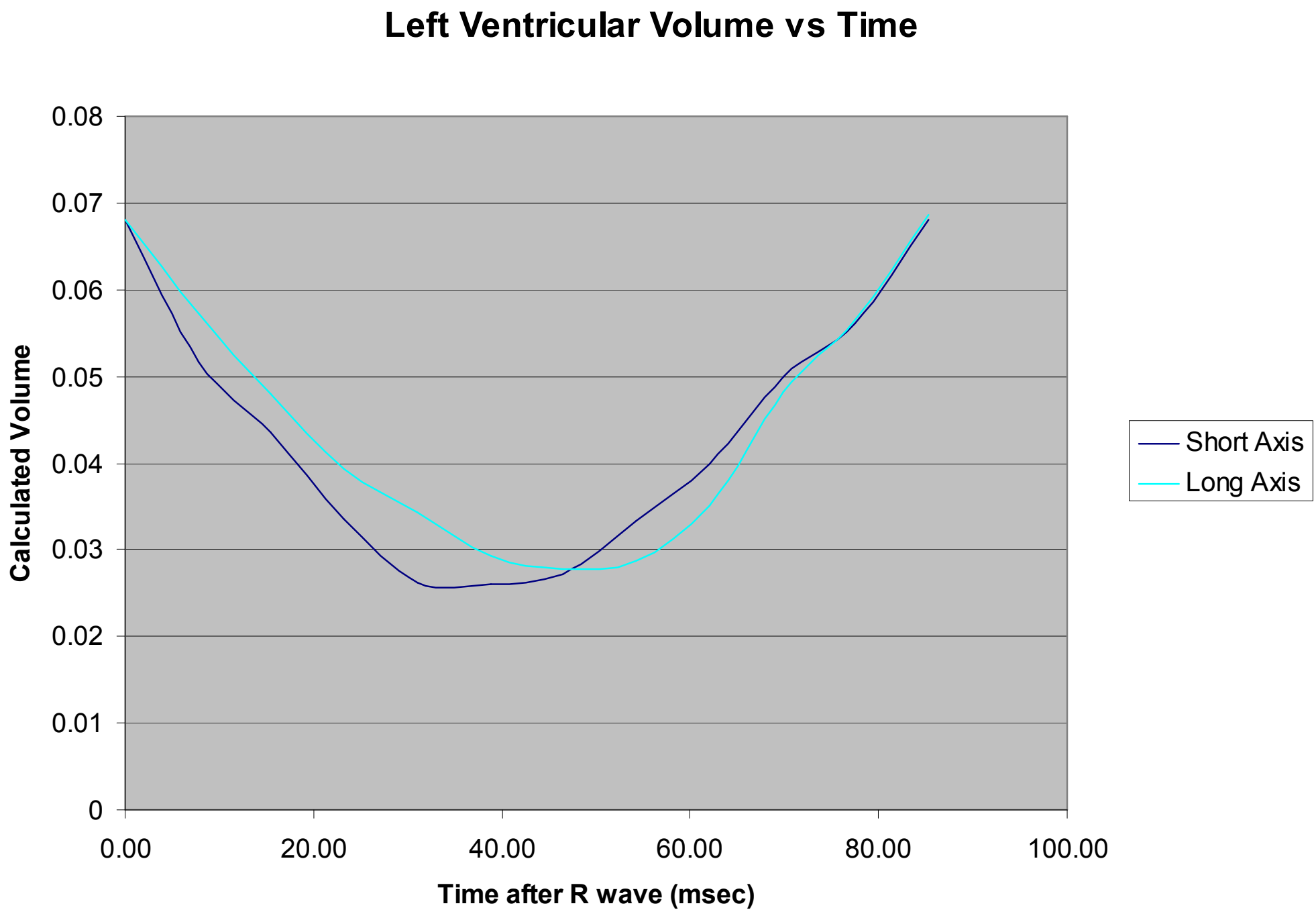
Part of right ventricle missing

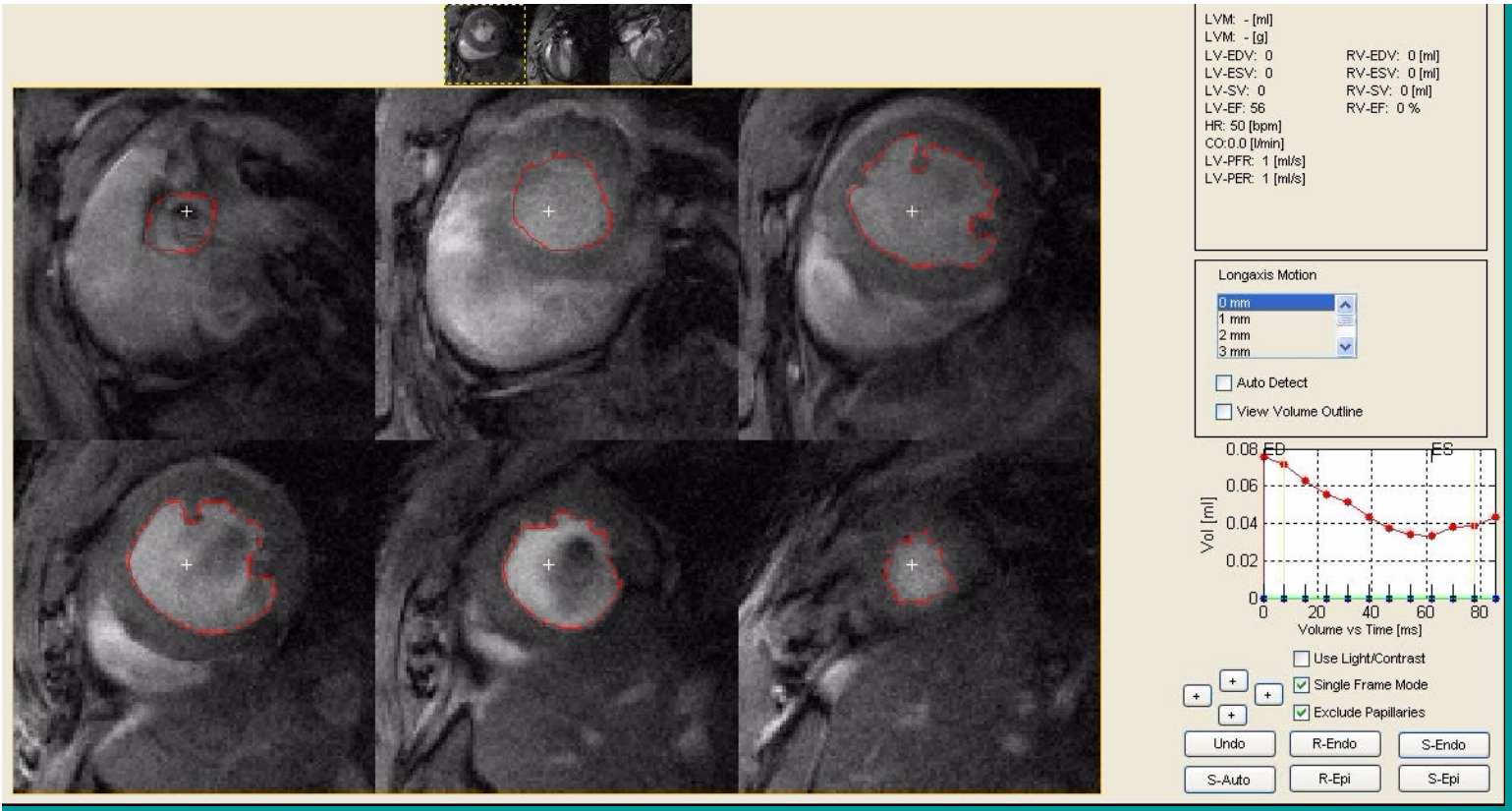




Short-axis acquisitions – underestimate right ventricular volume…




Left Ventricular Volume vs Time
Calculated Volume
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0.00
20.00
40.00
60.00
80.00
100.00
Time after R wave (msec)
Short Axis
Long Axis



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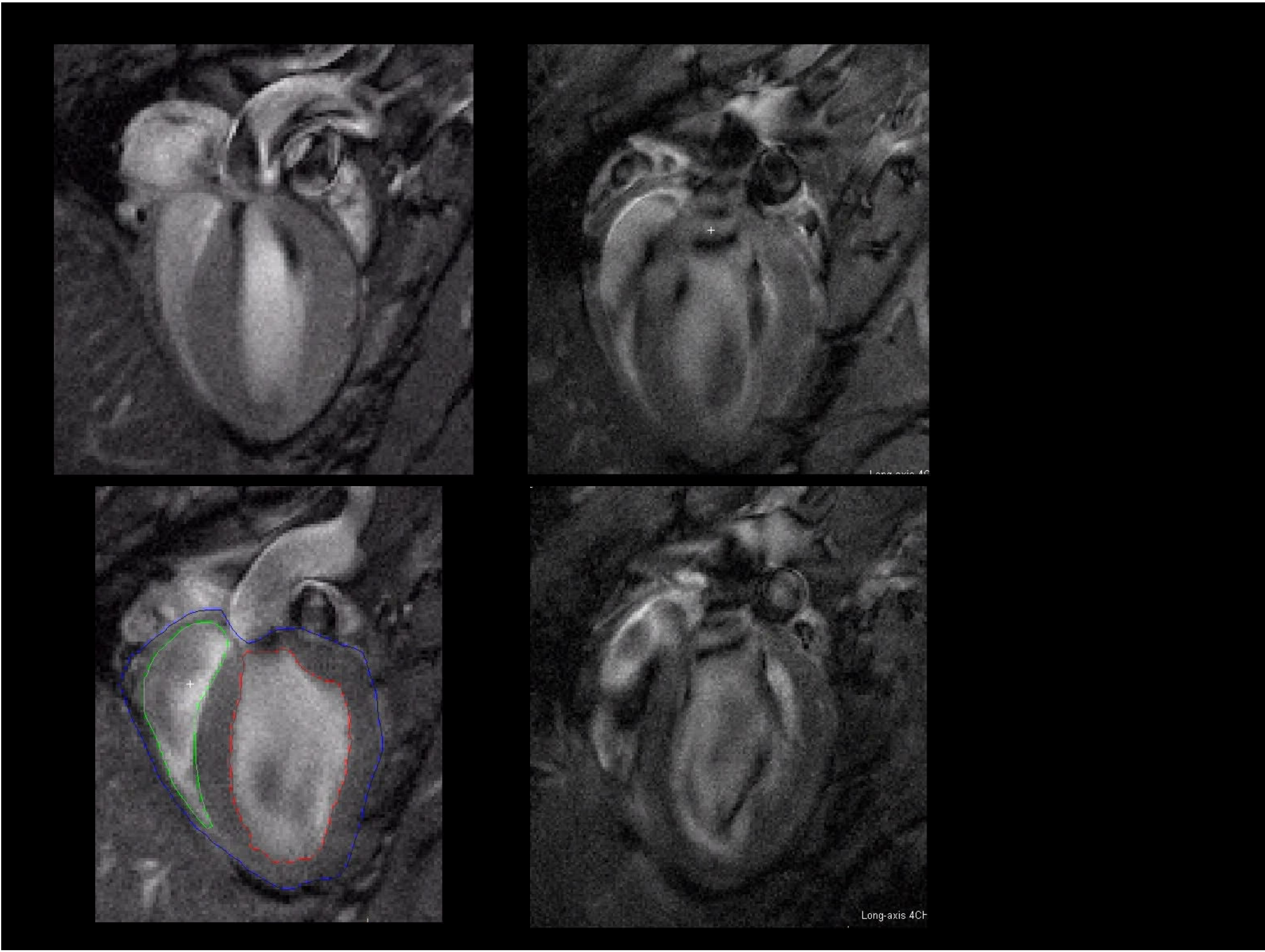
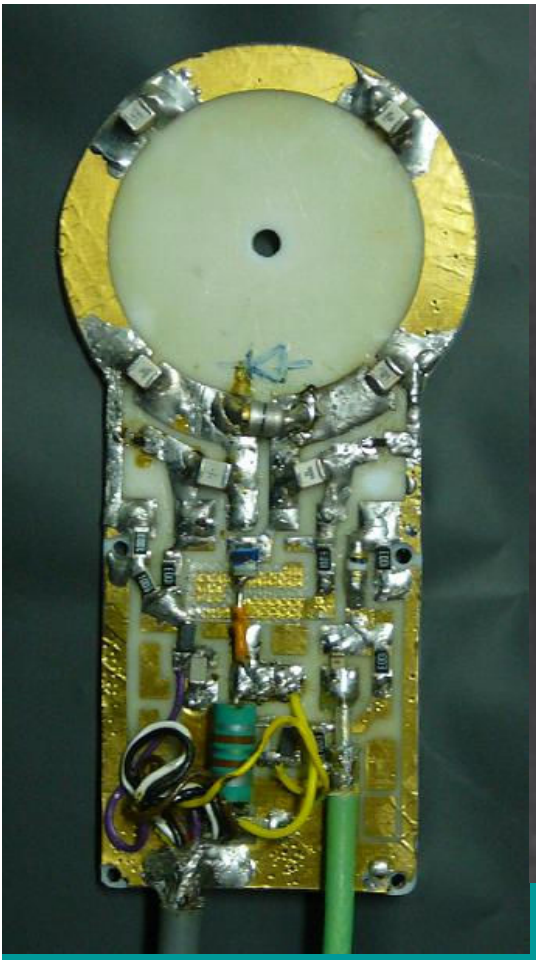
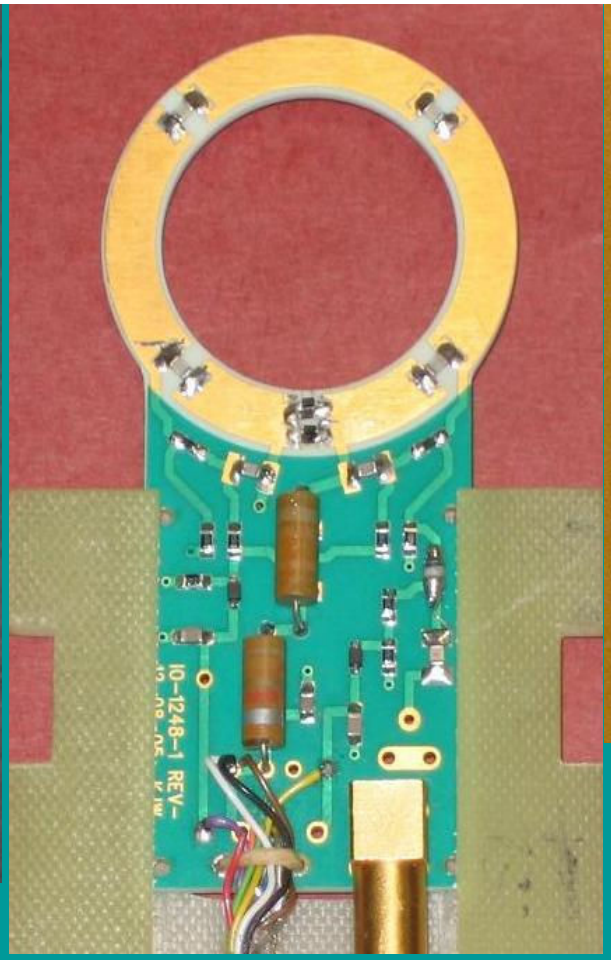
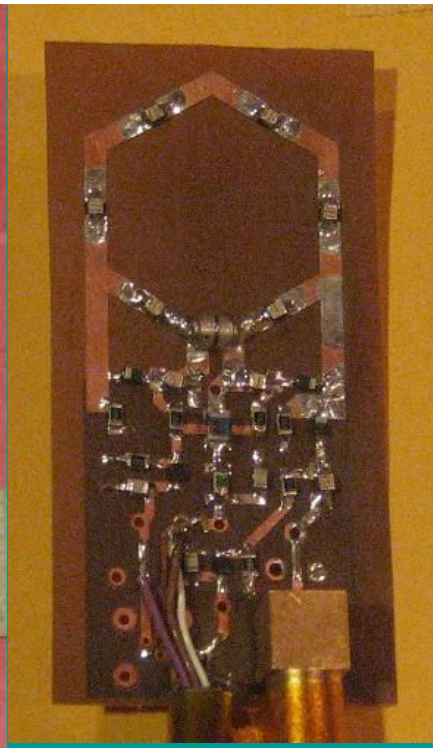

Long-axis 4CH

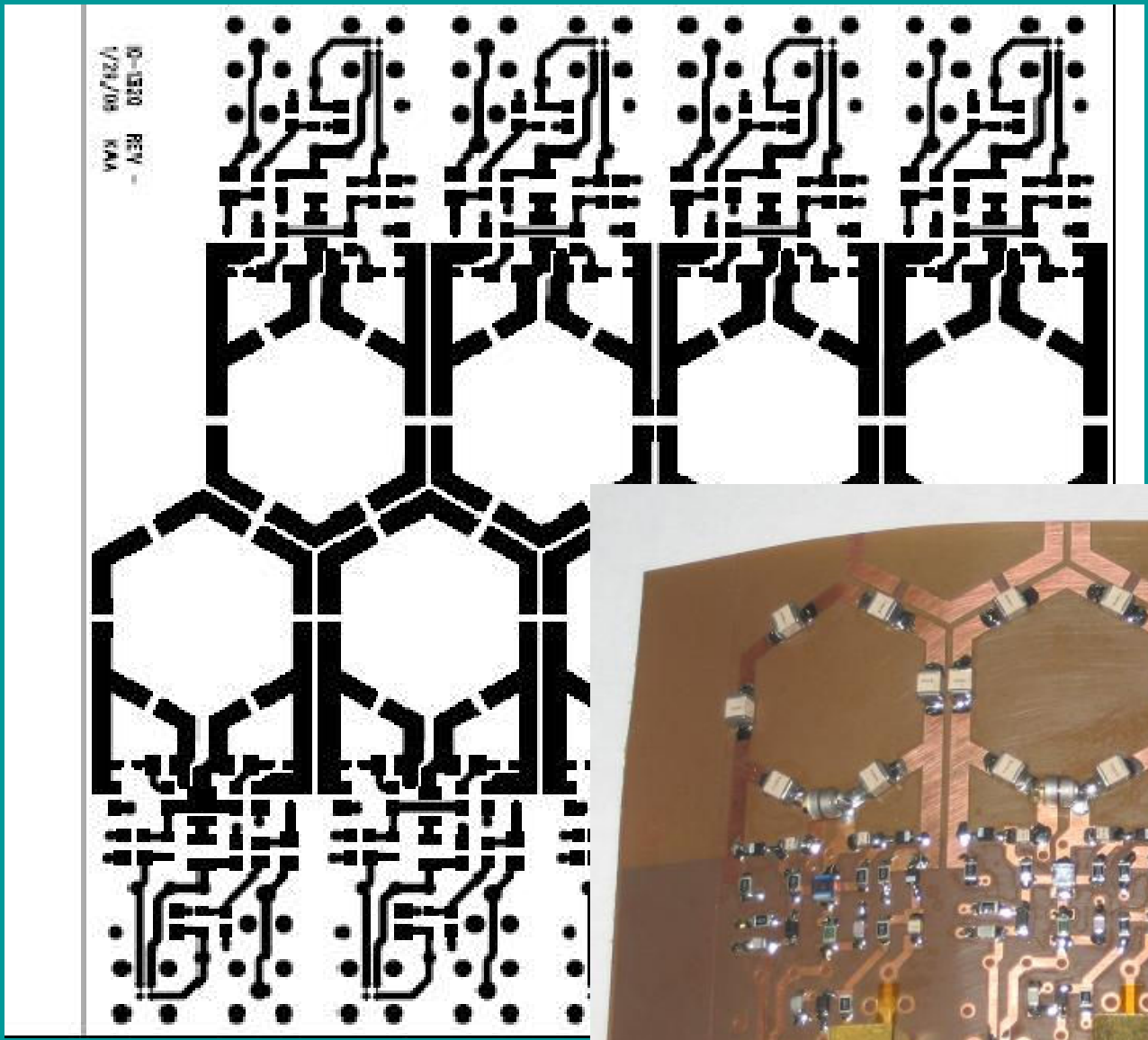


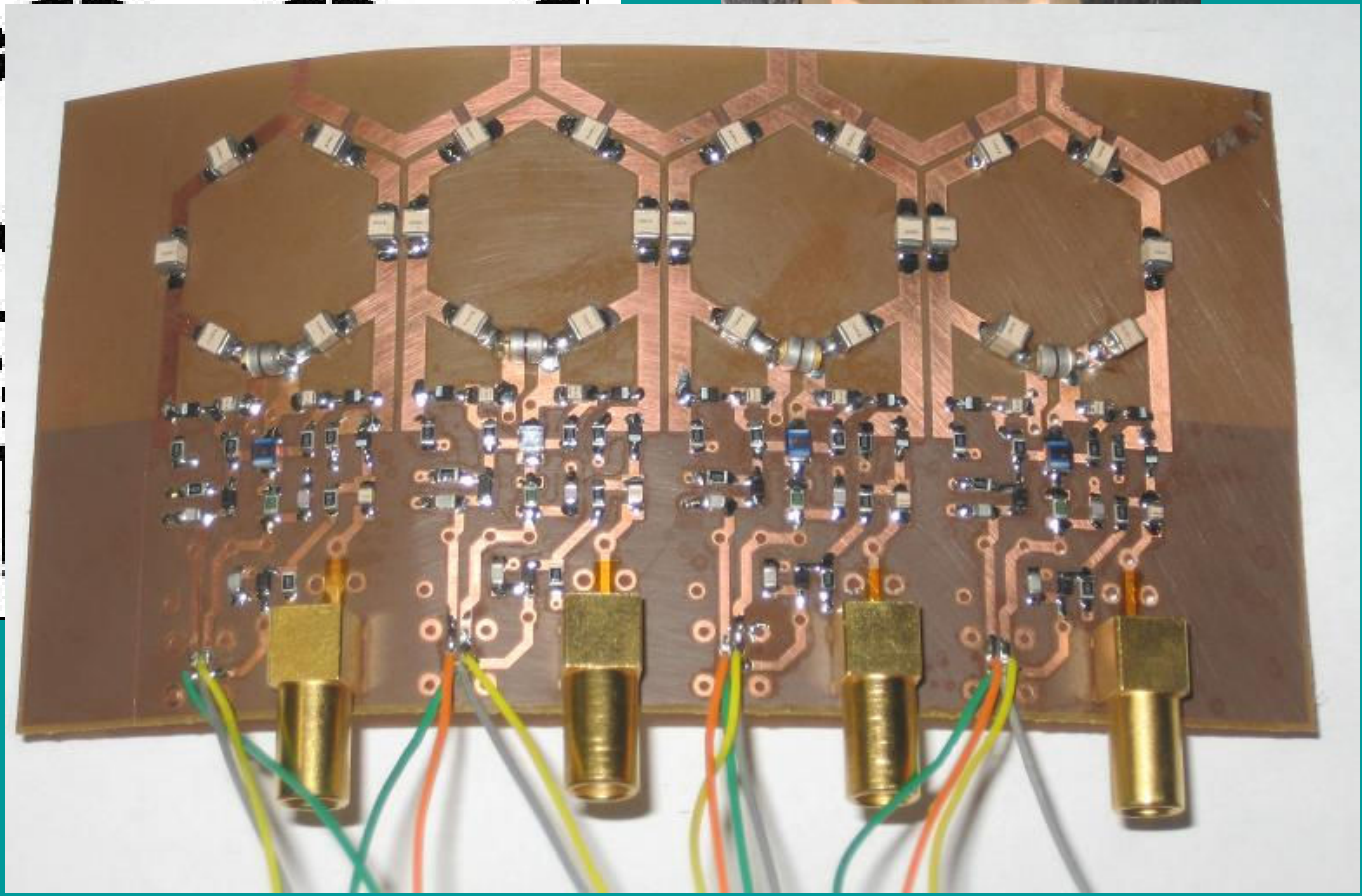




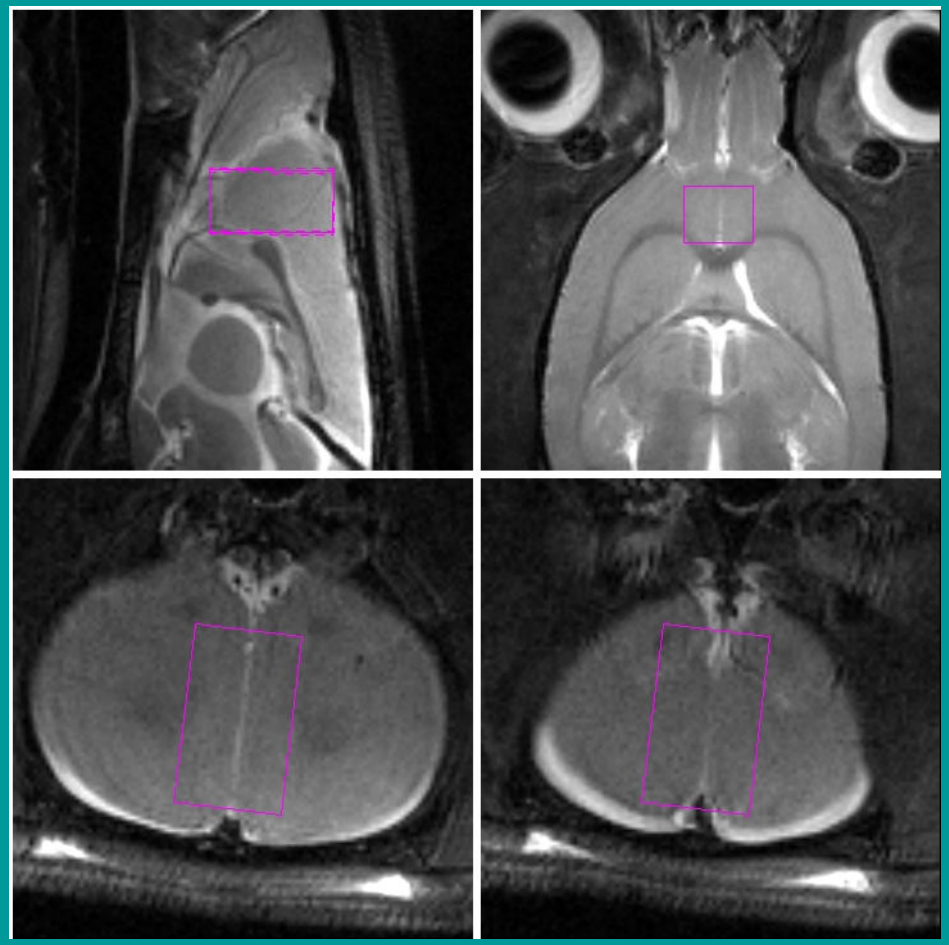
- Replicate existing coil designs with incremental improvements:

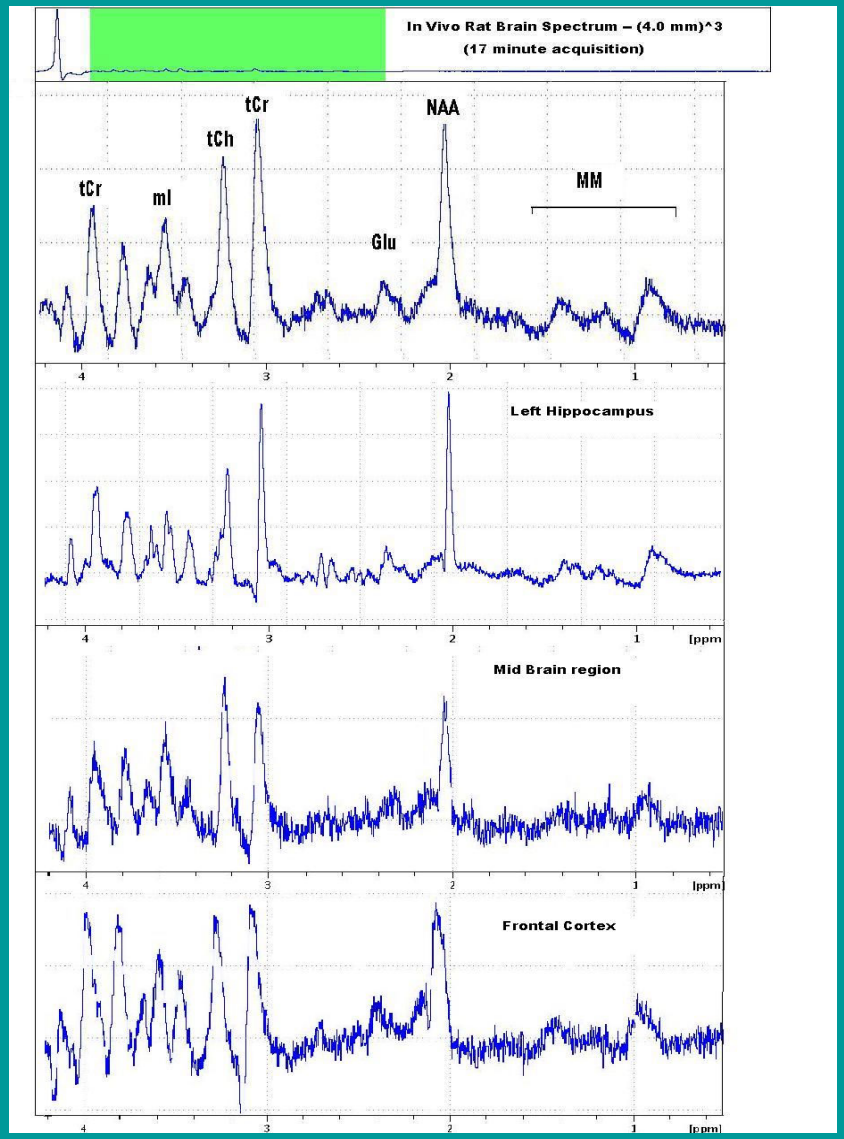
- Use better fabrication methods
- Investigate alternative components and
- modified tuning/matching & decoupling approach

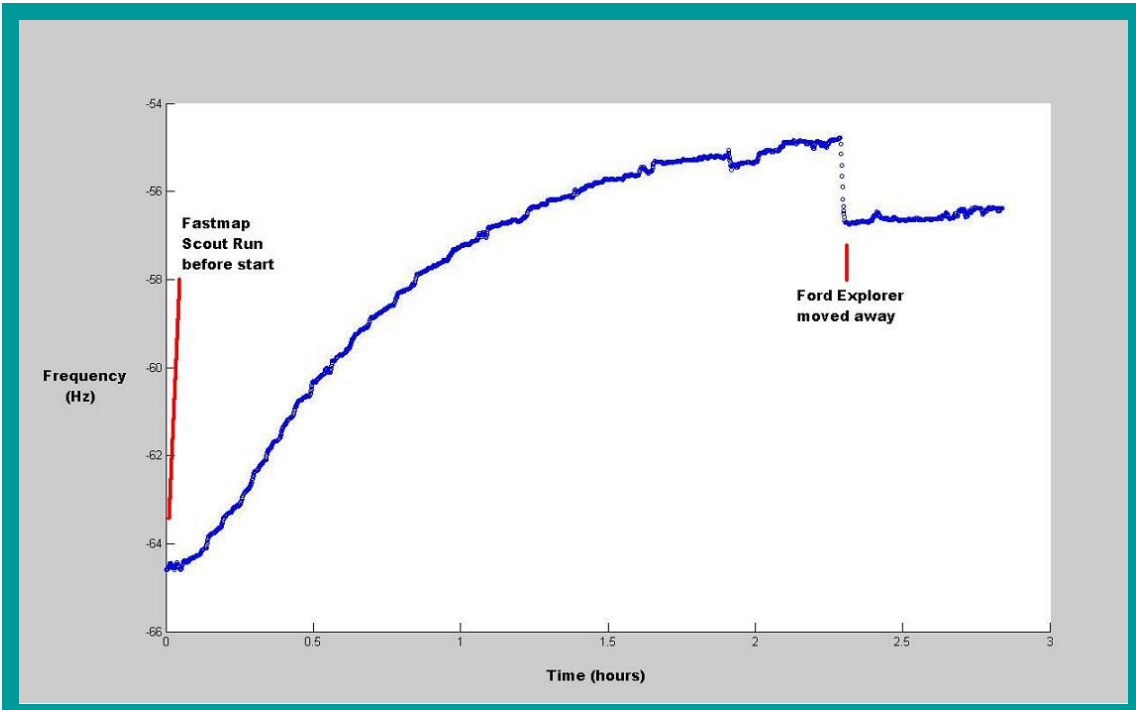

D-1500 REV -
1/28/08 KWA

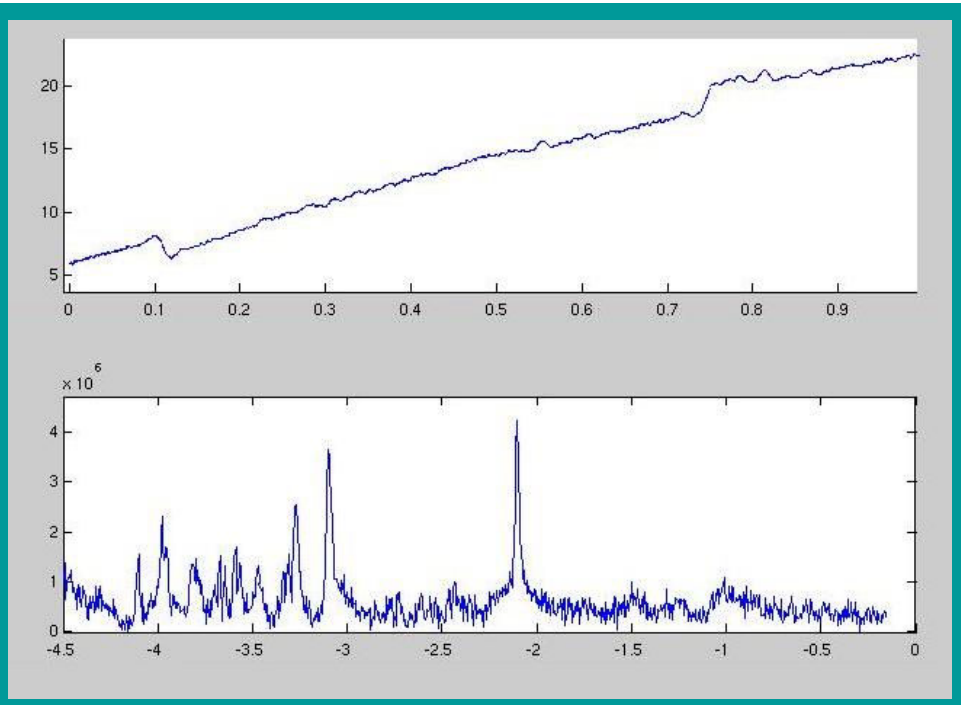


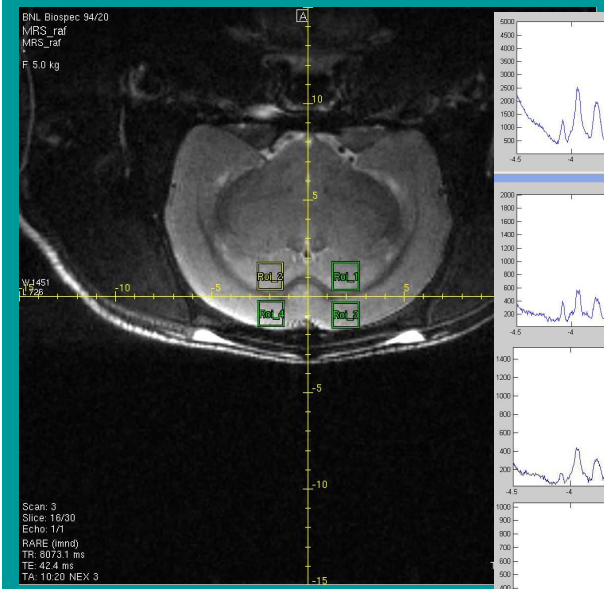
Chemistry of different brain regions

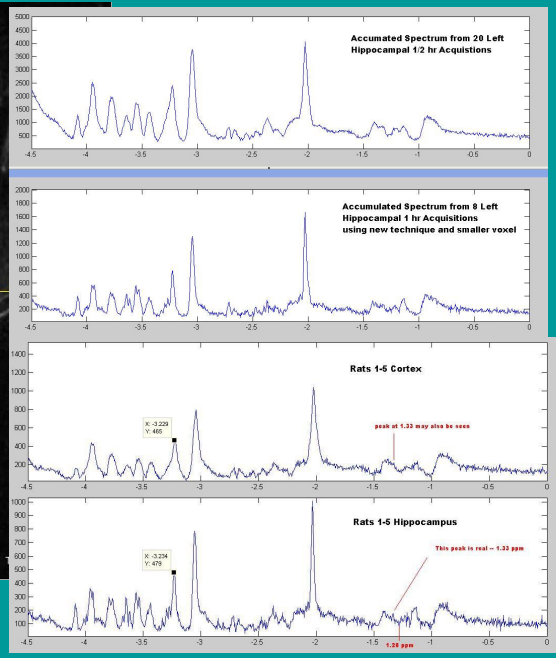


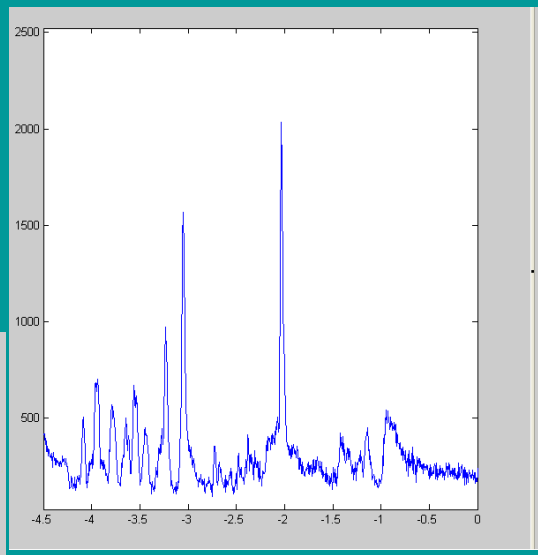


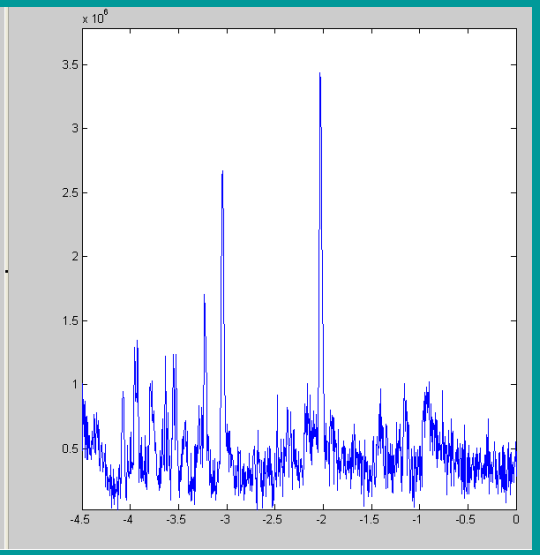

Fastmap
Scout Run
before start
Ford Explorer
moved away
Frequency
(Hz)
Time (hours)

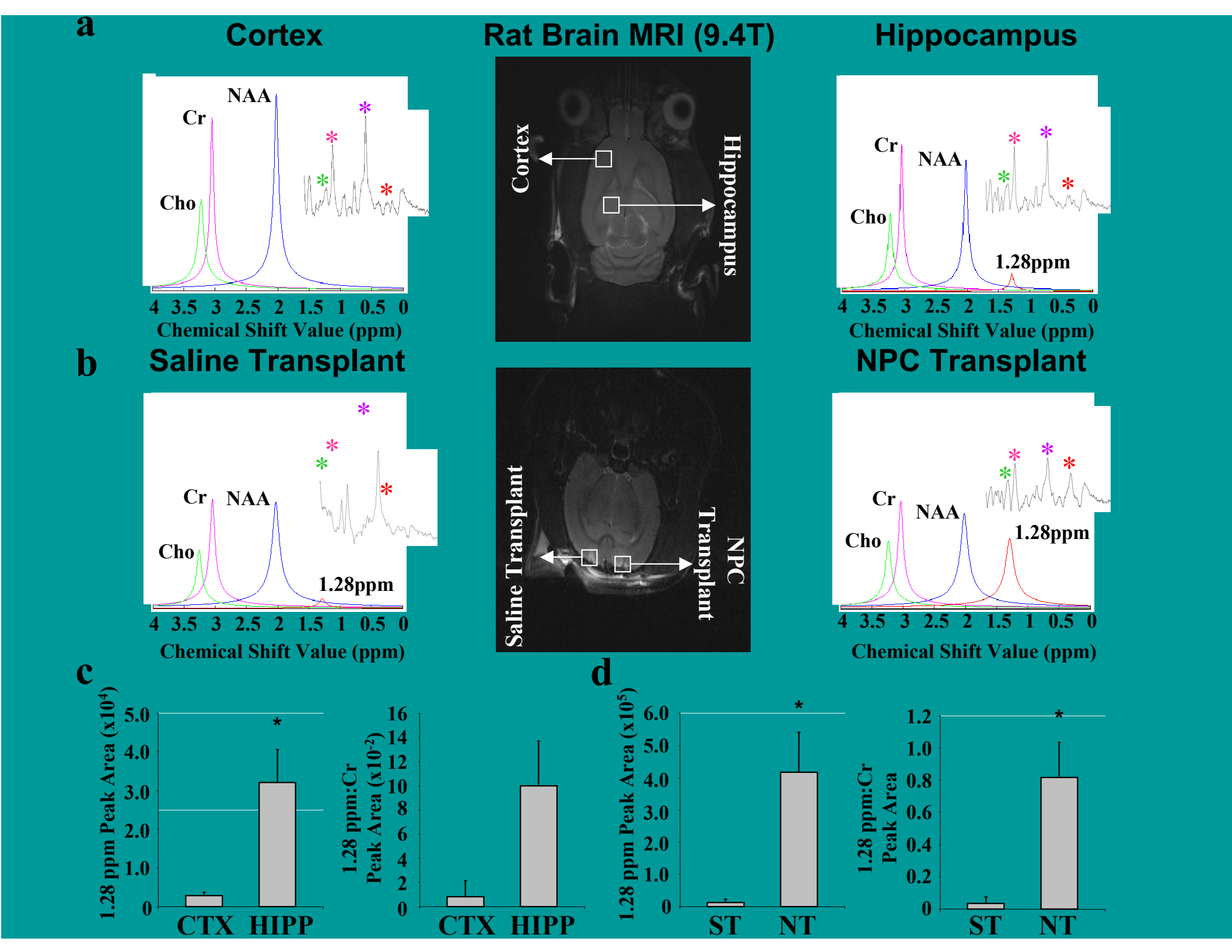



BNL Biospec 94/20
MRS_raf
MRS_raf
F 5.0 kg
Scan: 3
Slice: 16/30
Echo: 1/1
RARE (mnd)
TR: 8073.1 ms
TE: 42.4 ms
TA: 10:20 NEX 3

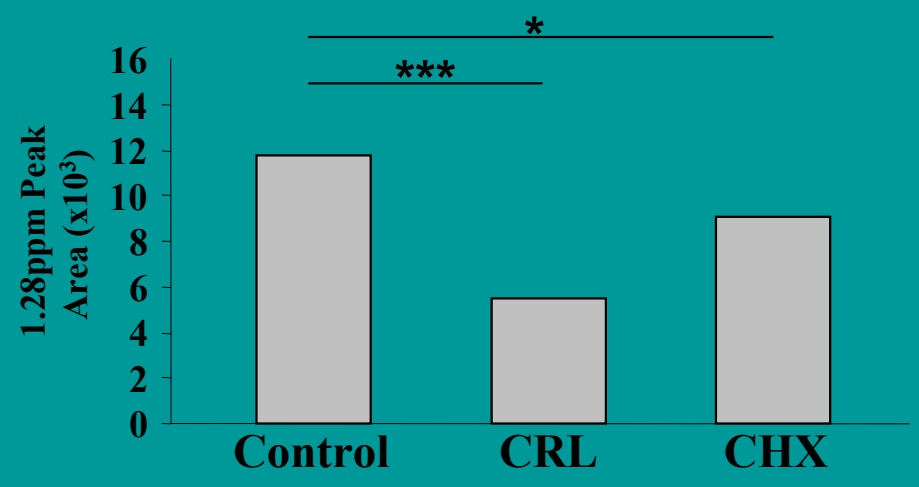

Accumated Spectrum from 20 Left
Hippocampal 1/2 hr Acquistions
Accumulated Spectrum from 8 Left
Hippocampal 1 hr Acquisitions
using new technique and smaller voxel
Rats 1-5 Cortex
peak at 1.33 may also be seen
Rats 1-5 Hippocampus
This peak is real – 1.33 ppm

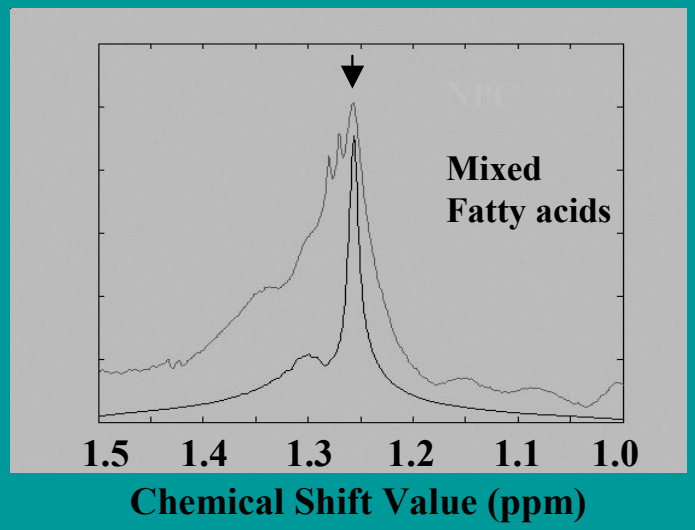





a
Cortex
Rat Brain MRI (9.4T)
Hippocampus
Cr
NAA
Cho
Cortex
Hippocampus
1.28ppm
4 3.5 3 2.5 2 1.5 1 0.5 0
Chemical Shift Value (ppm)
b
Saline Transplant
NPC Transplant
Saline Transplant
NPC Transplant
c
d
1.28 ppm Peak Area (x10^4)
1.28 ppm:Cr Peak Area (x10^-2)
1.28 ppm Peak Area (x10^5)
1.28 ppm:Cr Peak Area
CTX HIPP
ST NT

Chemical nature of the metabolite that produces the 1.28 ppm NPC peak ?



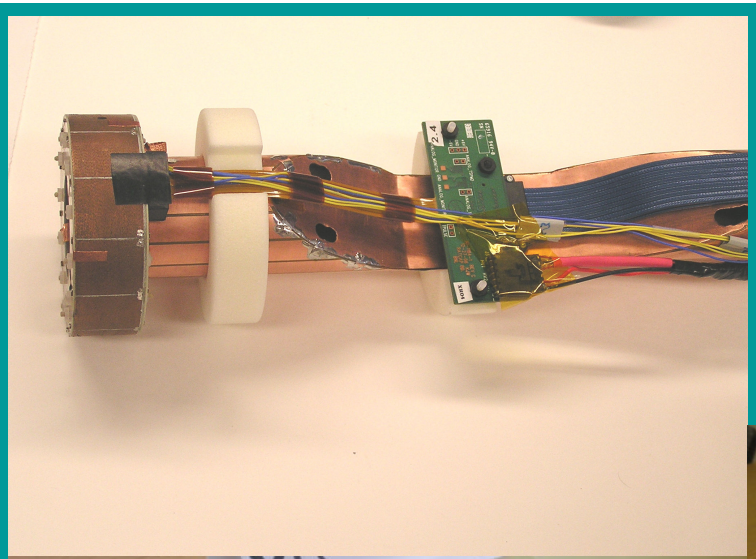


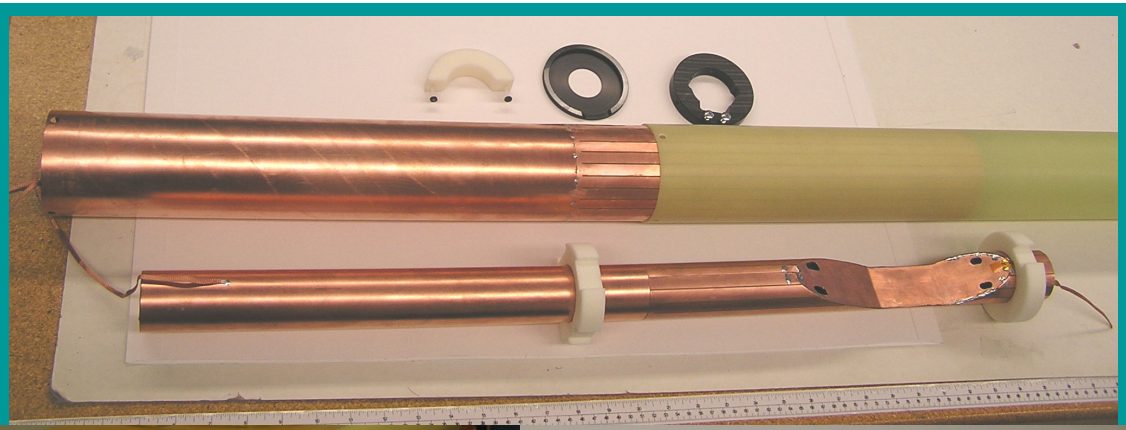
CRL=Cerulenin: (antifungal antibiotic isolated from *Cephalosporium caerulens*. Irreversibly binds to fatty acid synthase.

CHX=Cycloheximide: Protein synthesis inhibitor

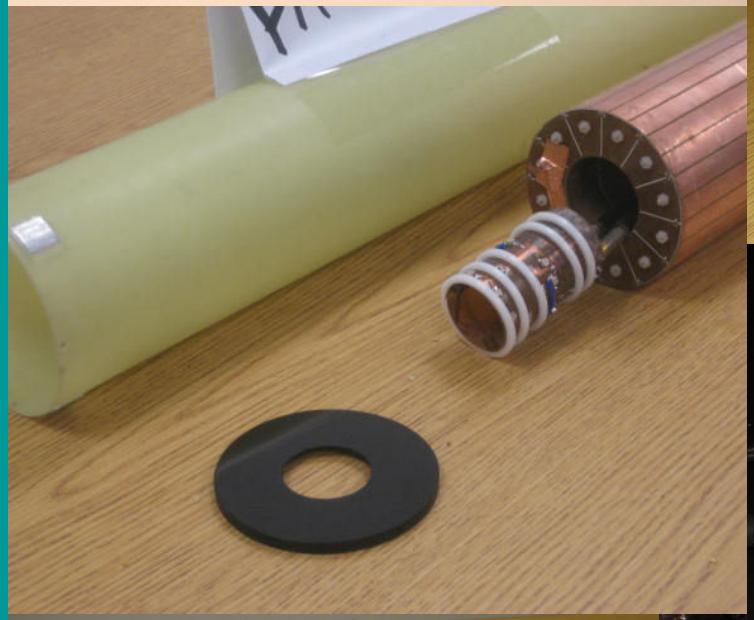
…….1H-NMR spectra of saturated fatty acids, such as palmitic and myristic acids overlapped with the 1.28 ppm peak

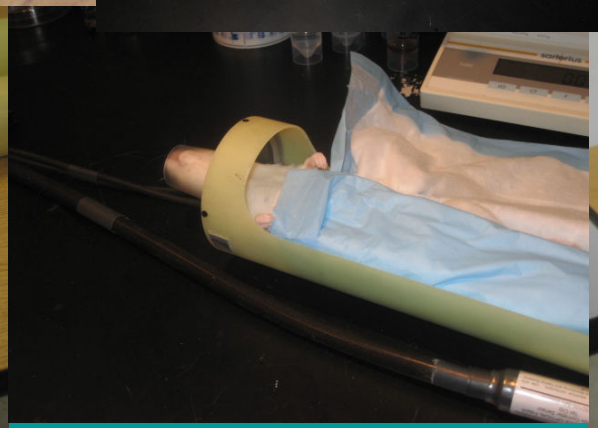
Maletic-Savatic et al., 2007

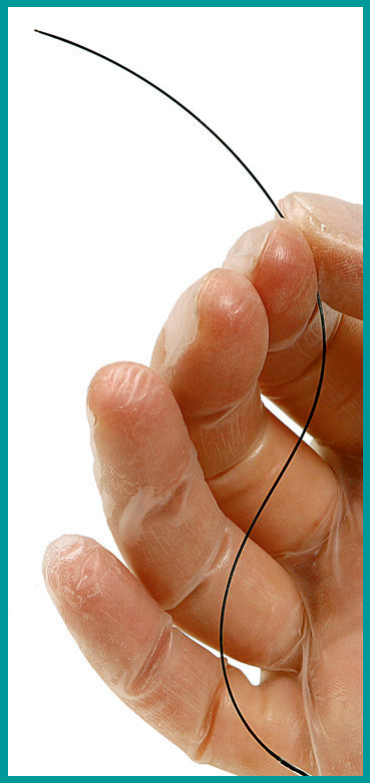


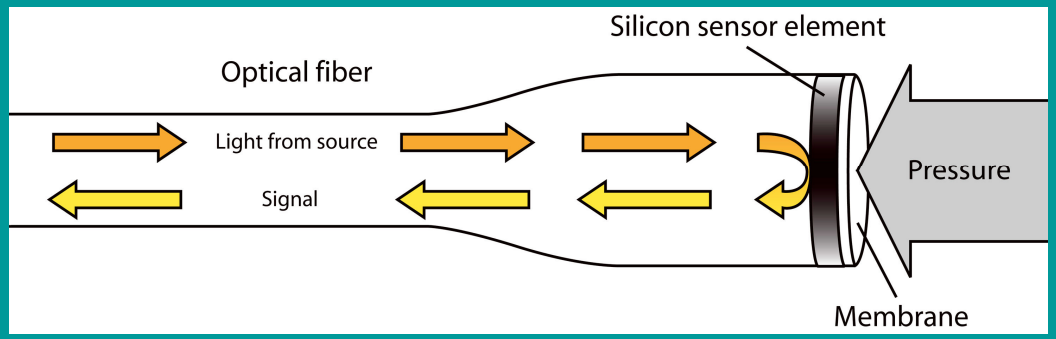


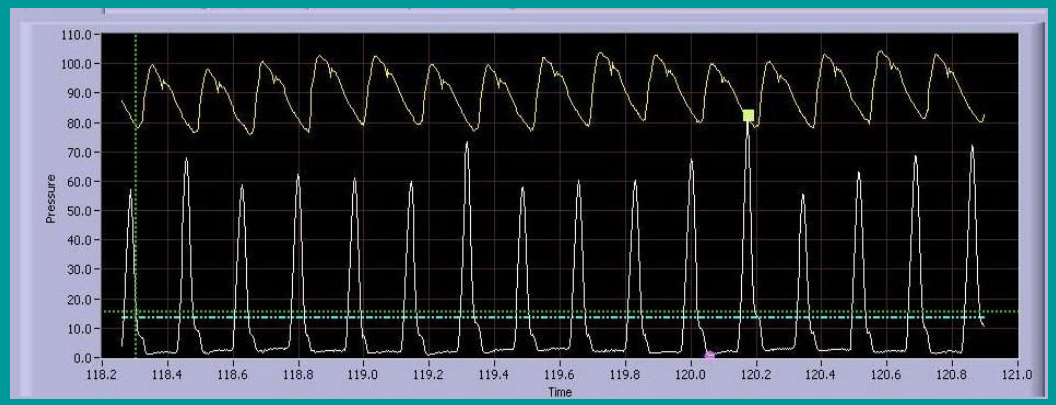
magnex
scientific

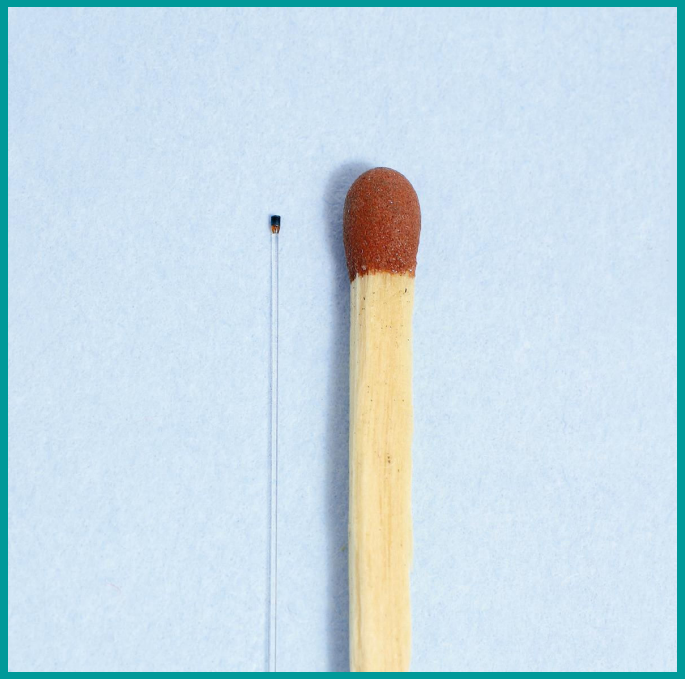


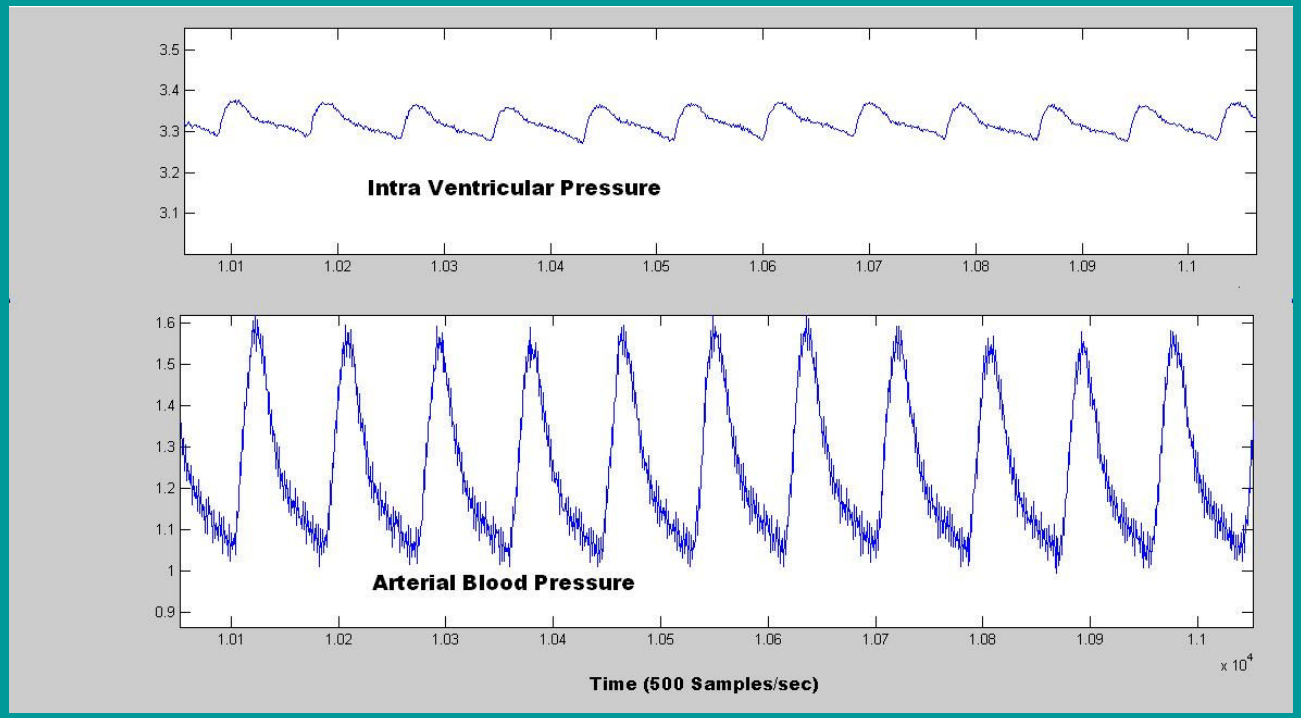





Silicon sensor element
Optical fiber
Light from source
Signal
Pressure
Membrane

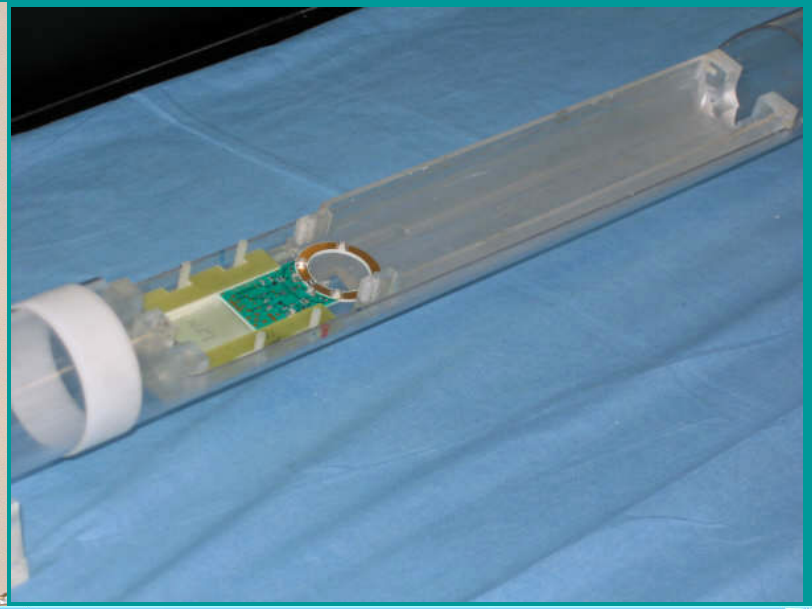

Pressure
Time




Intra Ventricular Pressure
Arterial Blood Pressure
Time (500 Samples/sec)

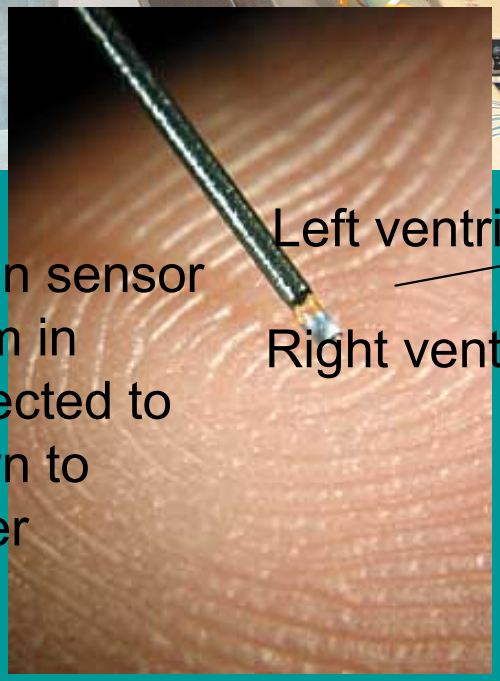
MR microscopy: Cardiac Physiology

Non-invasive

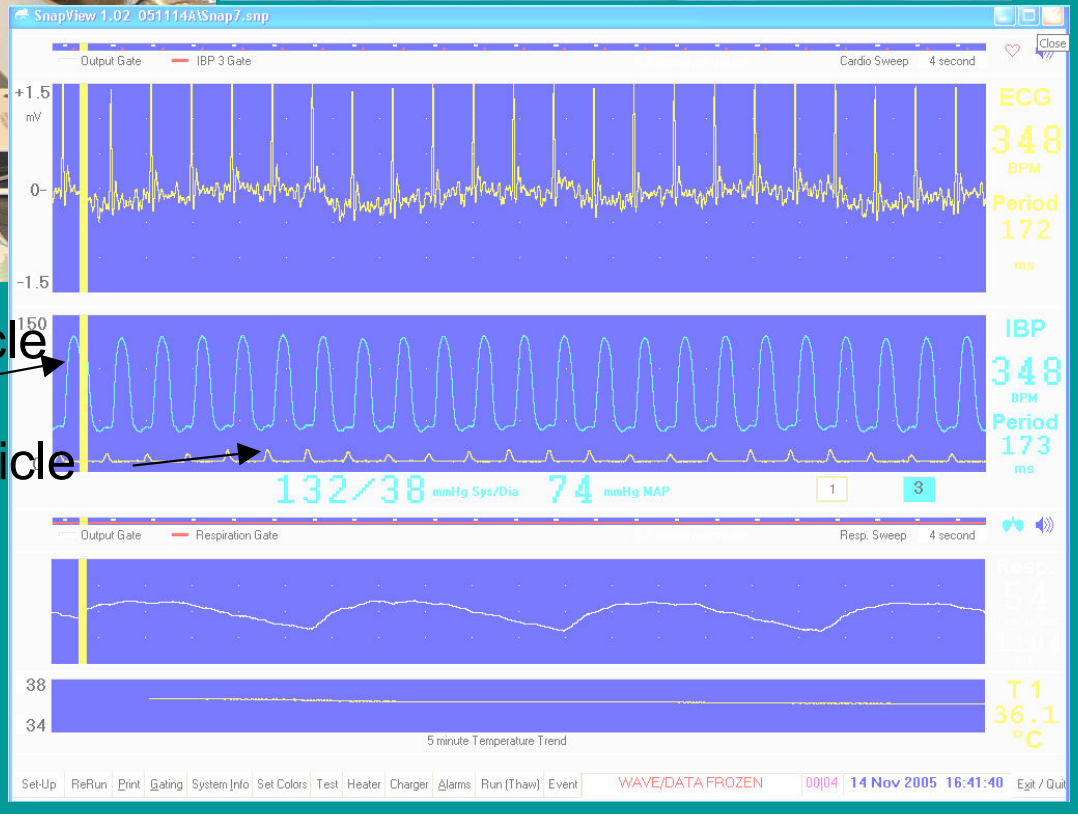


Invasive:

Micro Pressure Transducer into heart chambers



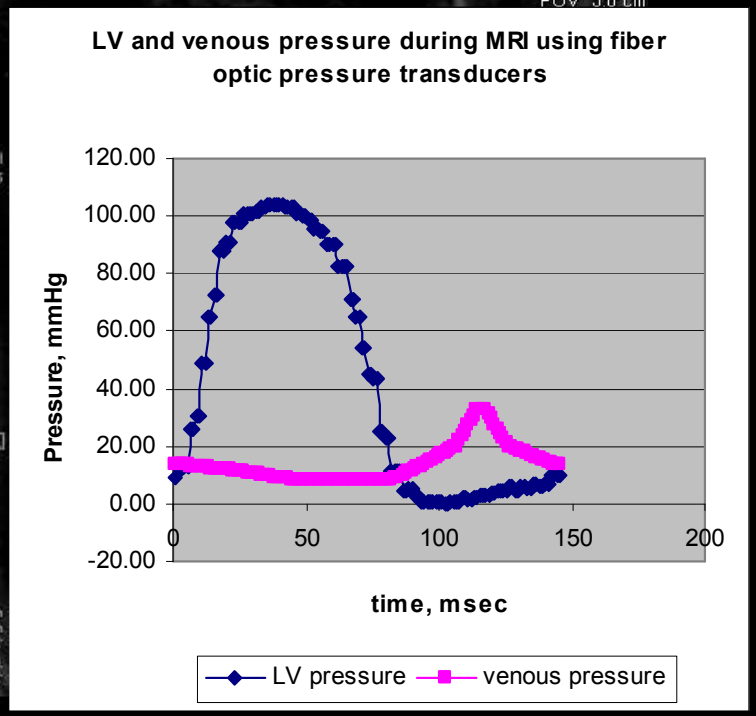
The sensor, a silicon sensor element, is 0.42 mm in diameter and connected to an optical fibre down to 0.25 mm in diameter
Samba, Sweden



Left ventricle

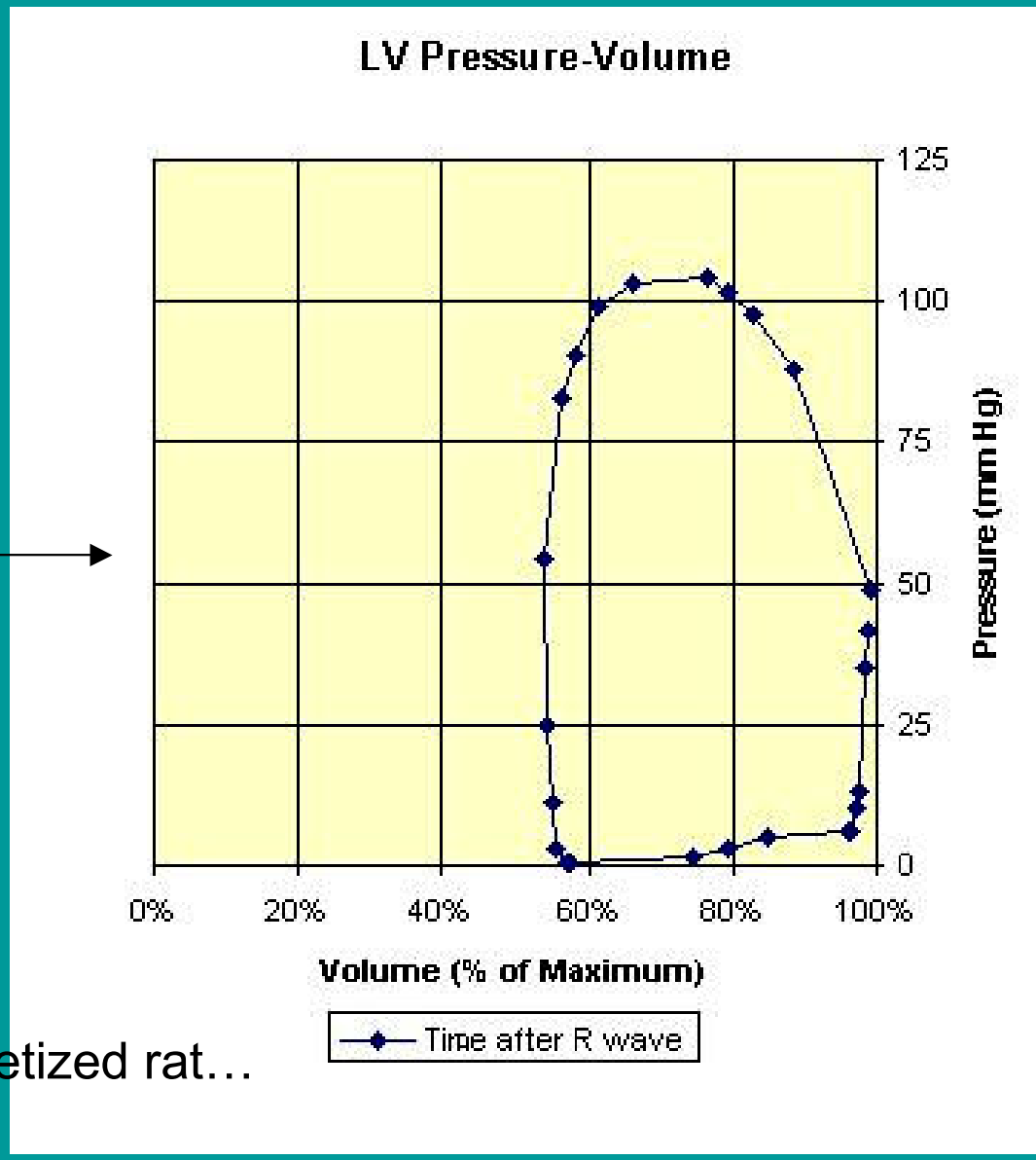
Right ventricle

Cardiac phenotyping

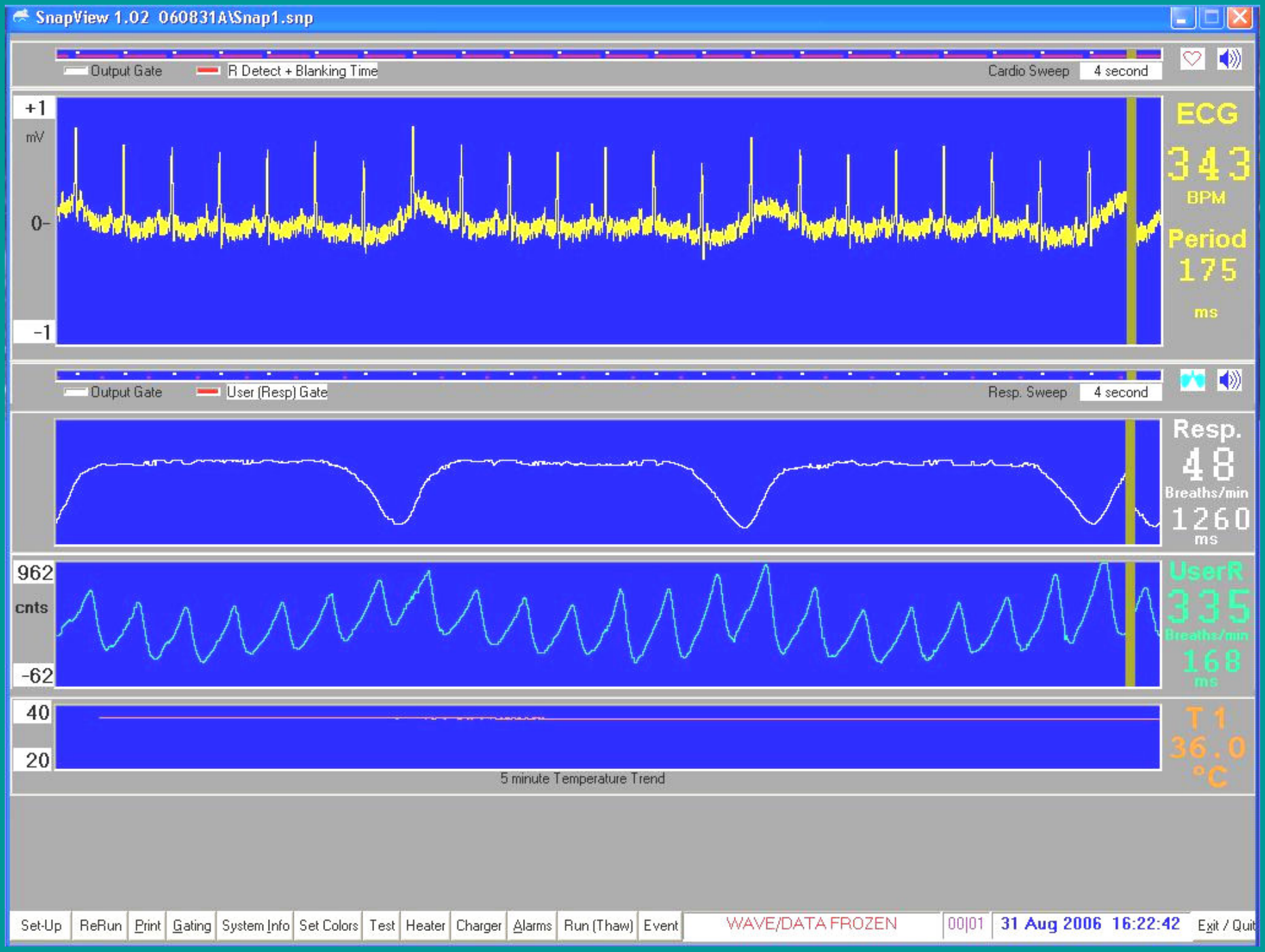


Smith and Benveniste, 2006

Cine…….



3000 heart beats to create movie…….
On average 3-400 bpm in a living anesthetized rat…
….approximately 5min

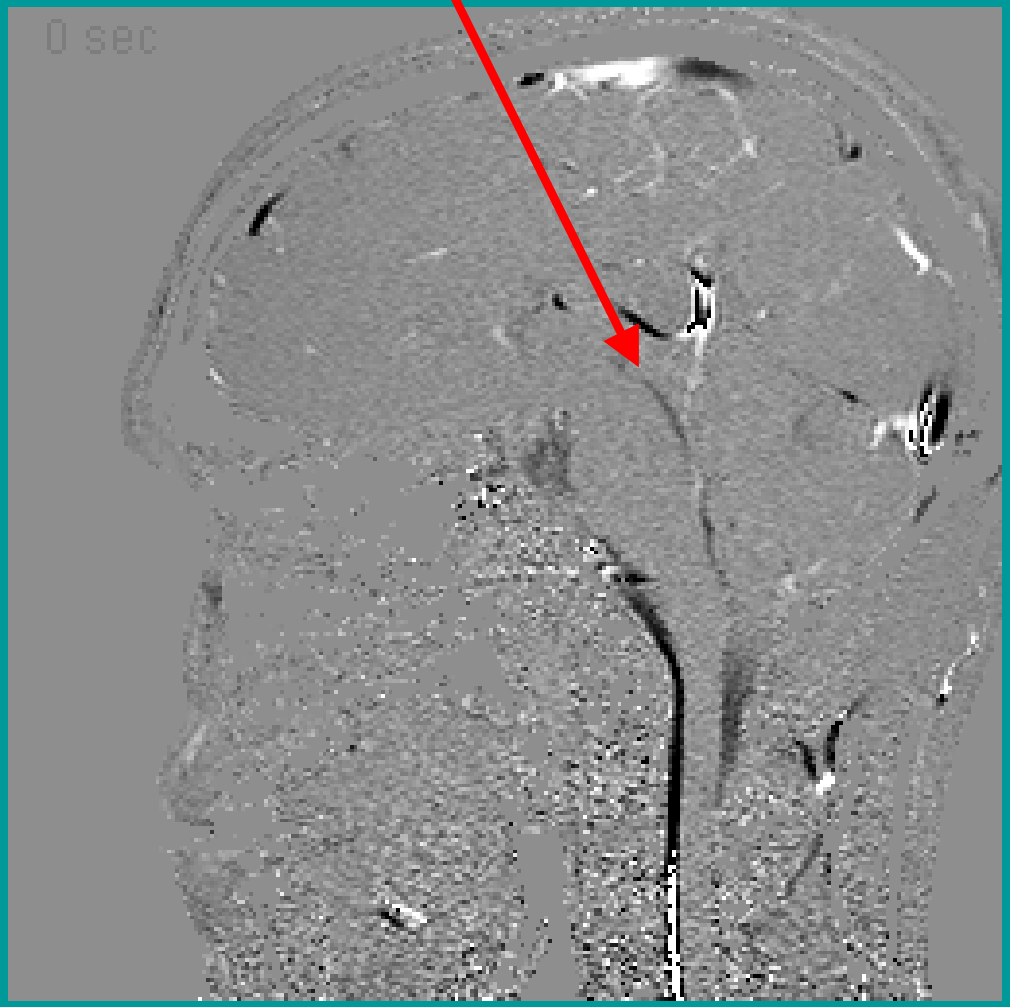


With MR gradients running….

Smith et al., 2006

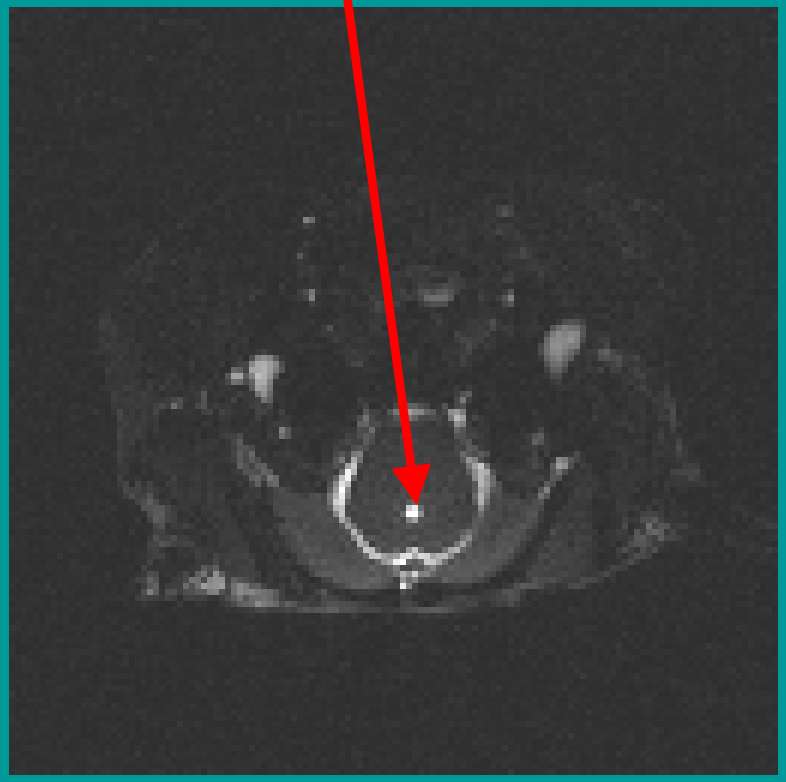
Cardiac-gated MRI measurement of pulsatile CSF flow

Human aqueduct:
1-2 mm in diameter



Pulsatile CSF flow
~ 30 μl/heart beat

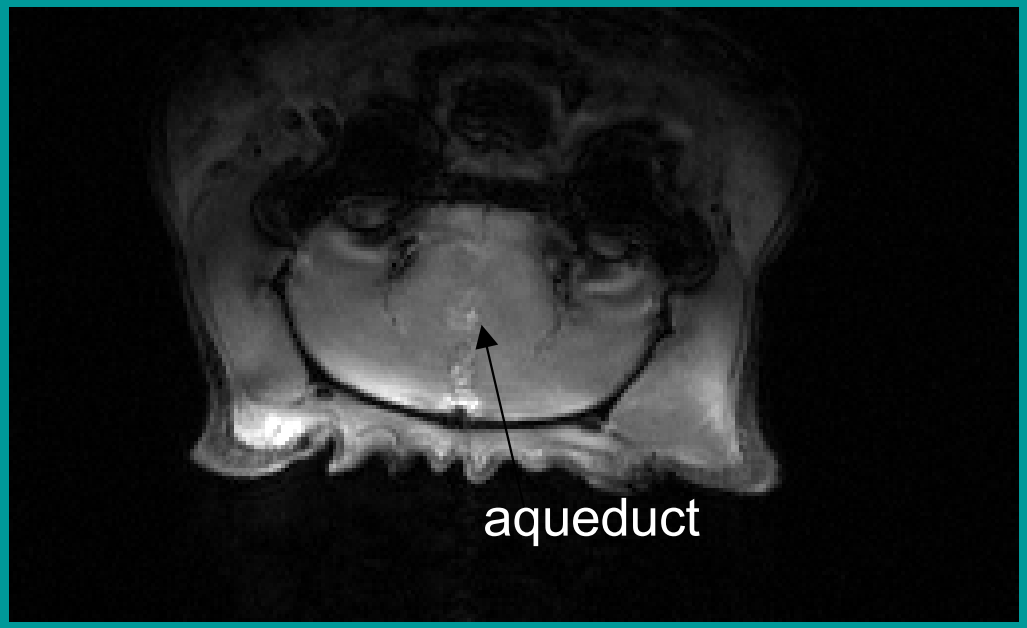
Rat aqueduct:
300μm in diameter



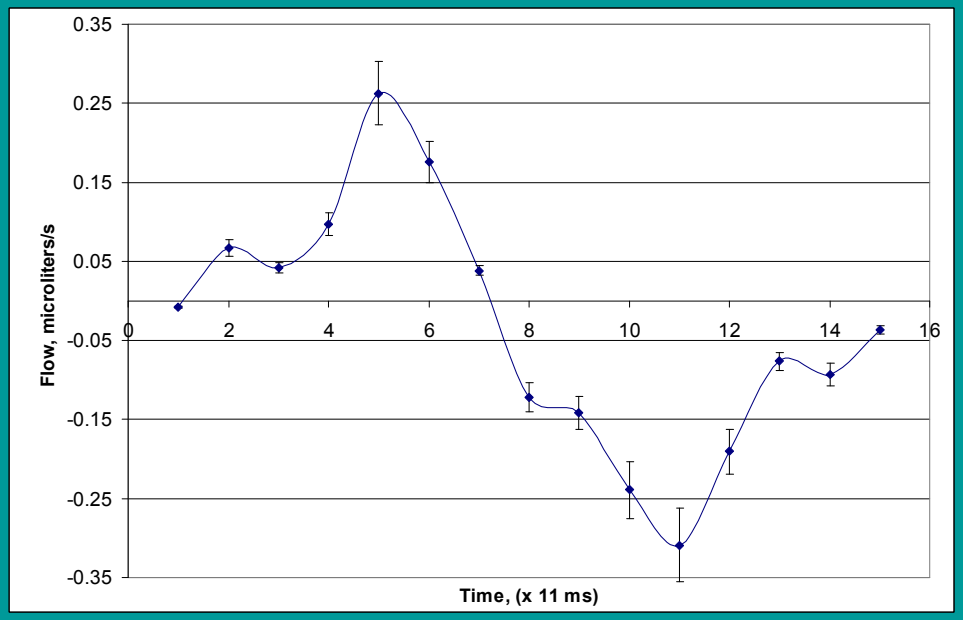
Pulsatile CSF flow
~ 10-20 nl/heart beat

Wagshul et al., 2006

Cardiac-gated MRI measurement of pulsatile CSF flow



PC-bSSFP image of the rat acqueduct



Measured CSF flow velocity in the aqueduct of a control rat.

Fully balanced steady state free precession phase contrast (PC-bSSFP) sequence

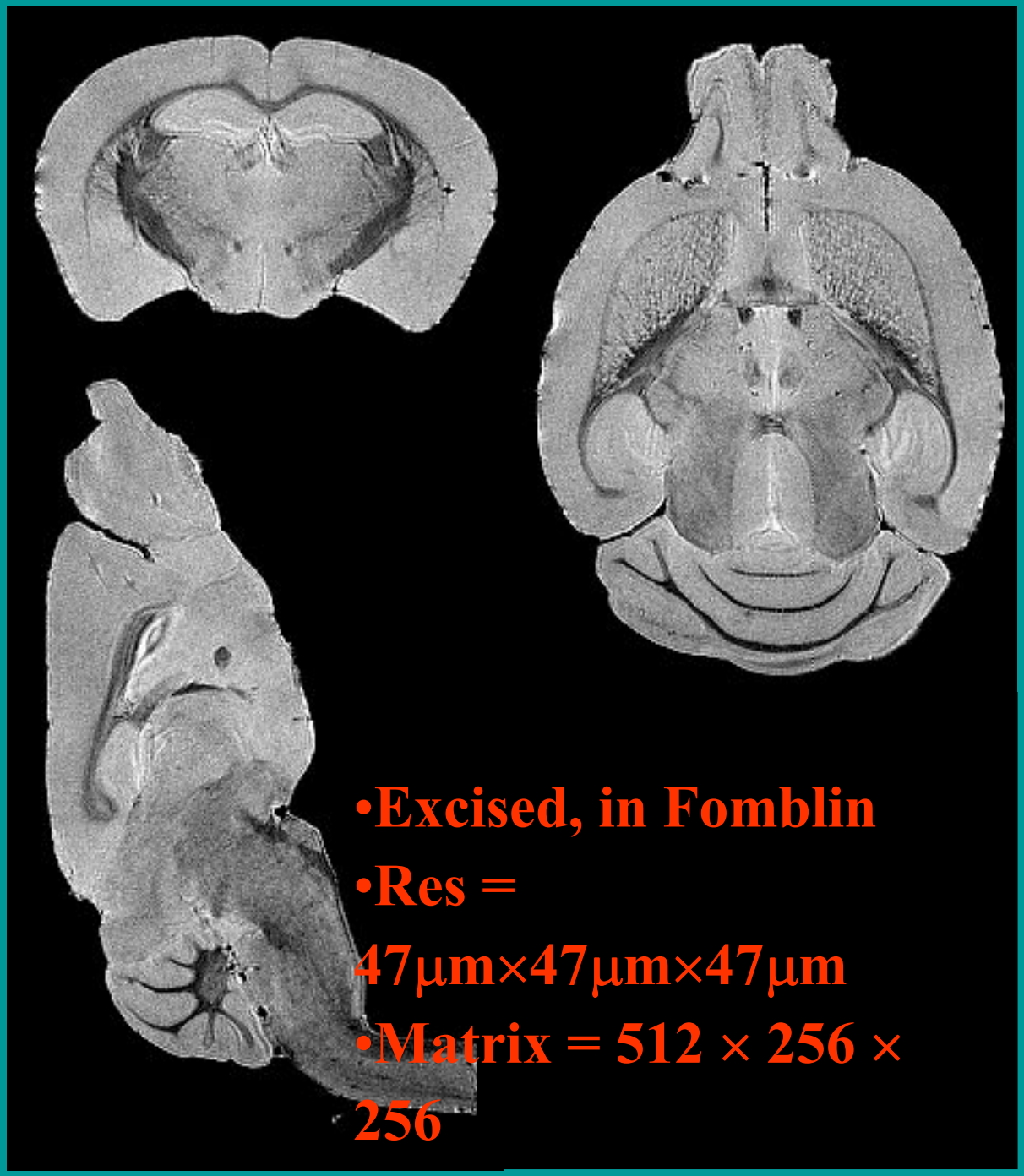
Wagshul, Egnor, Smith, Benveniste, in prep. 2006

MR Microscopy & Informatics

In collaboration with:

Dr. Yu Ma (SBU, BNL)
BNL ITD (Drs. Bennett, McGuigan, Slatest)
Dr. Stephen J. Blackband (UFL)
Dr. P. Hof (MSSM)

In Vitro Magnetic Resonance Microscopy



- Bruker (UFL): 17.6 T
- T2* Gradient Echo:

  TE=7.5ms;

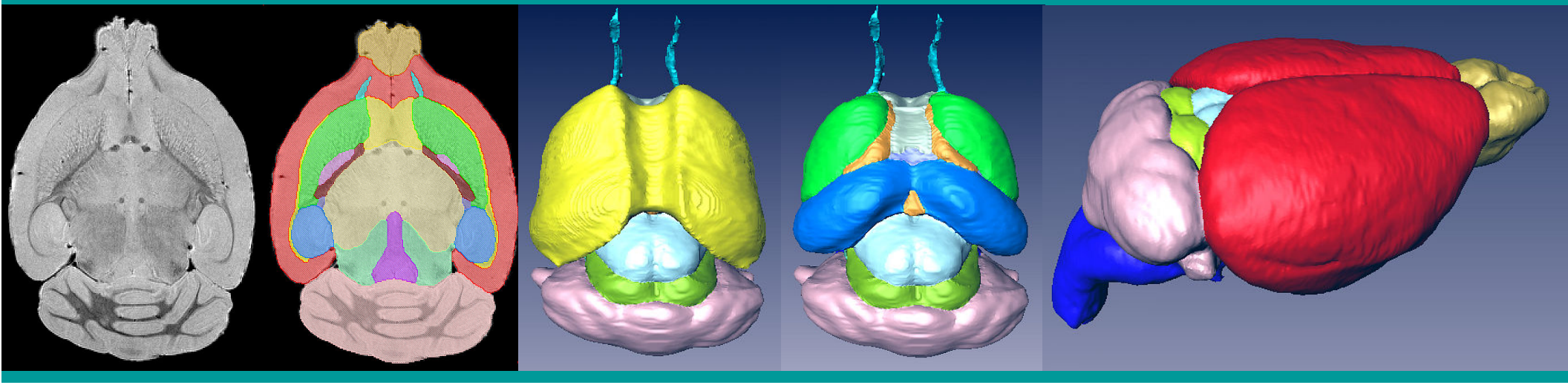
  TR=150ms;

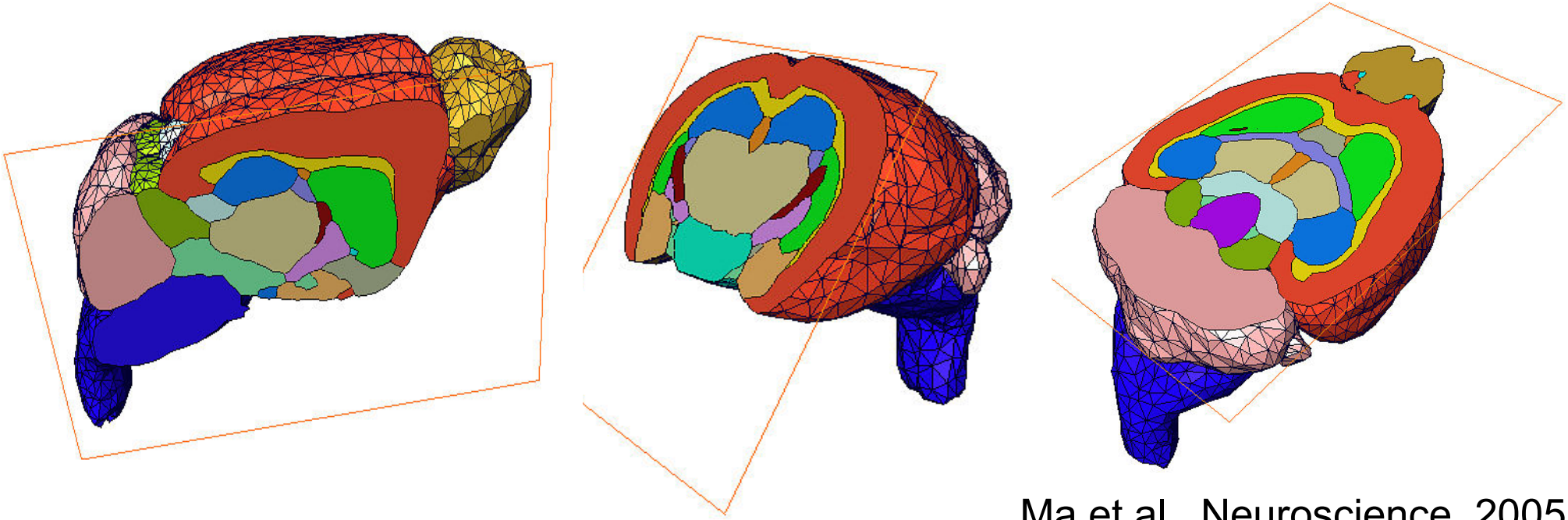
  FOV = 2.4x1.2x1.2cm;

  NEX = 2;

  AQT = 5.5hrs.

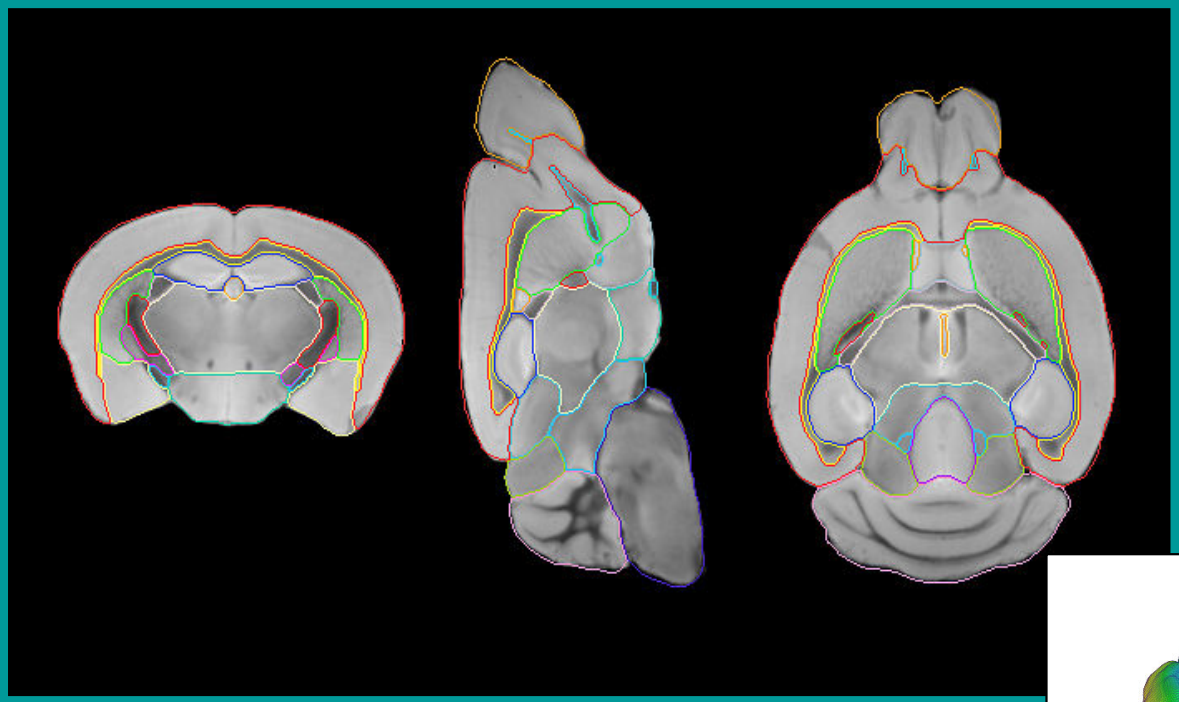
3D Normal Mouse Brain Atlas

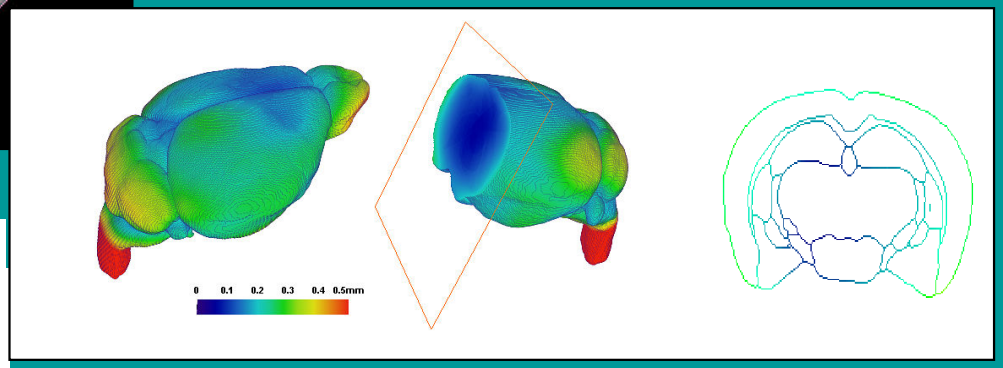


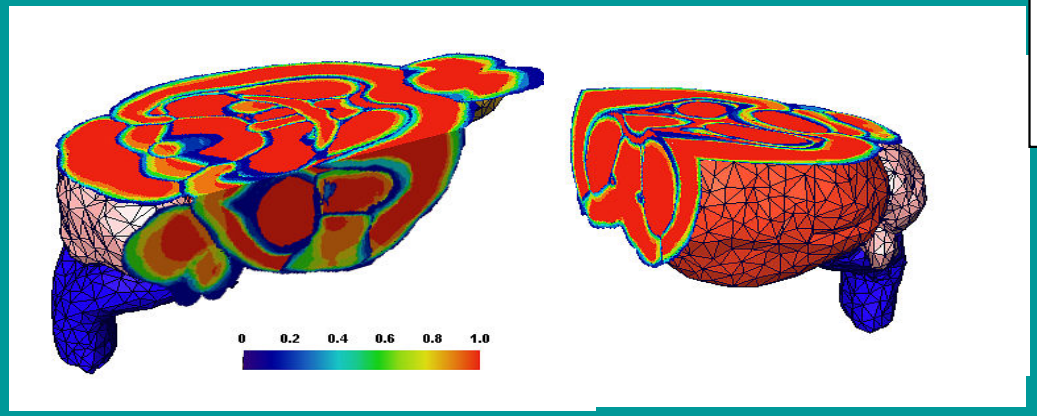


Ma et al., Neuroscience, 2005

Average Atlas and Probabilistic Atlas (n = 10)

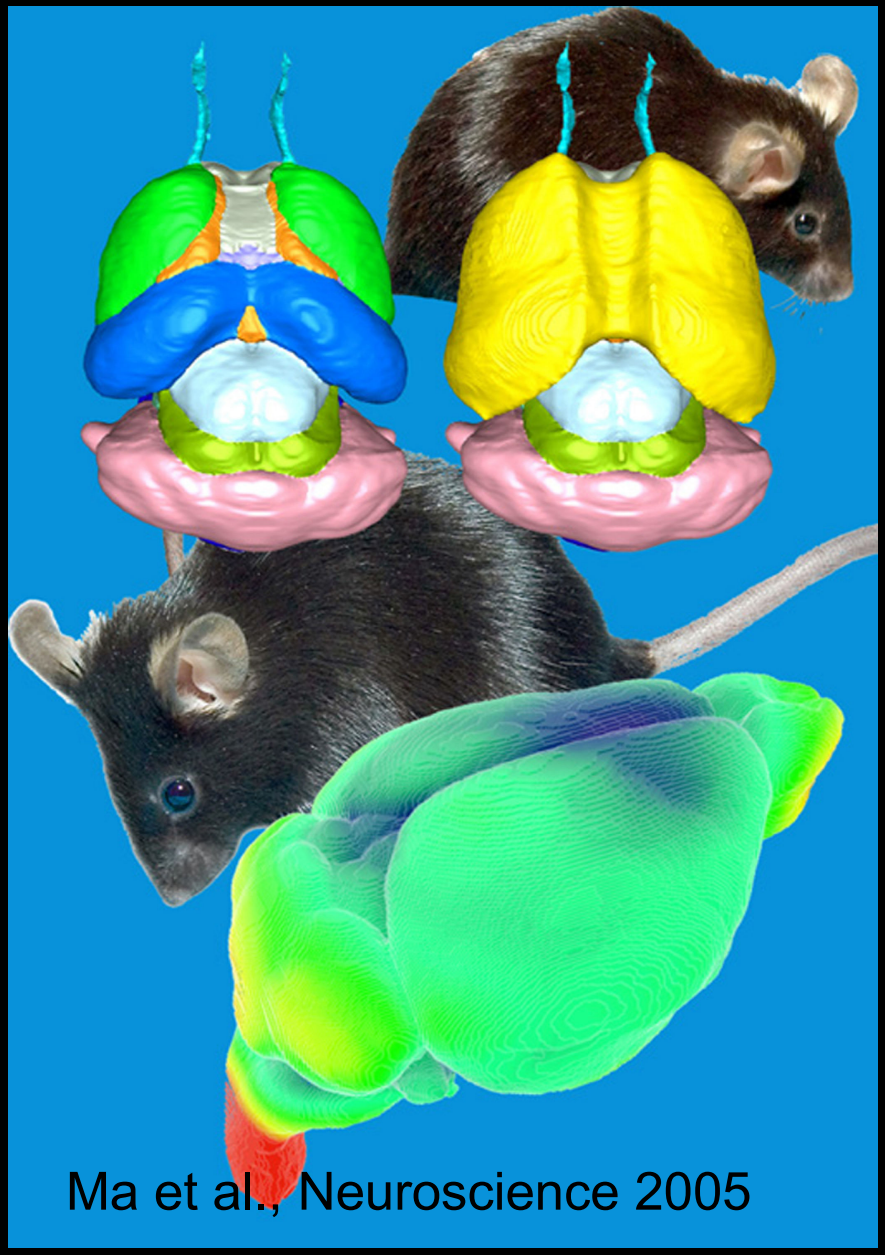






Ma et al., Neuroscience, 2005

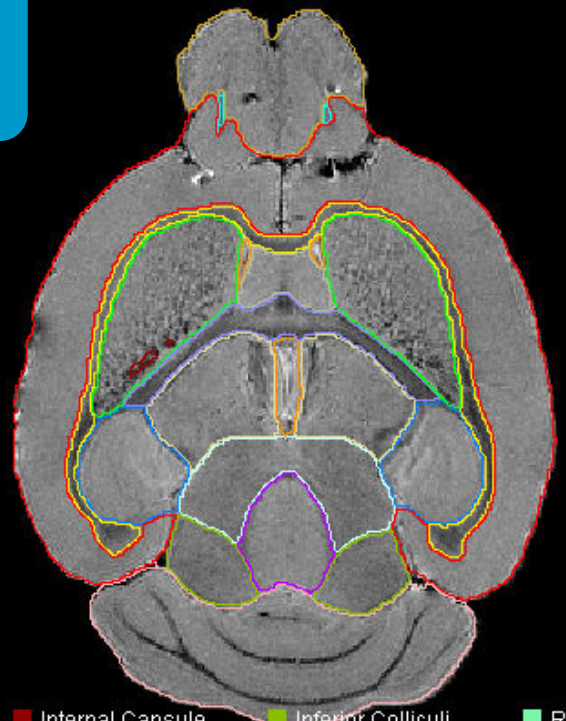
Quantitative Morphometry



Ma et al., Neuroscience 2005

www.bnl.gov/ctn/mouse

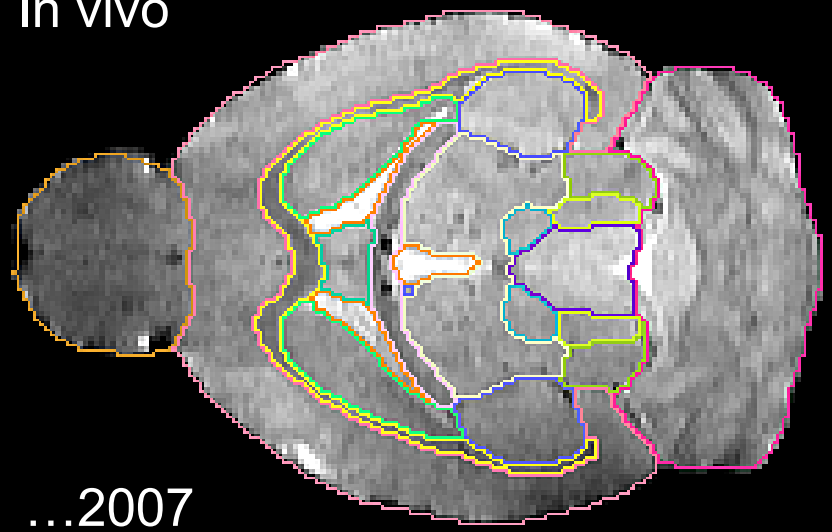
In vitro



Structure Names:

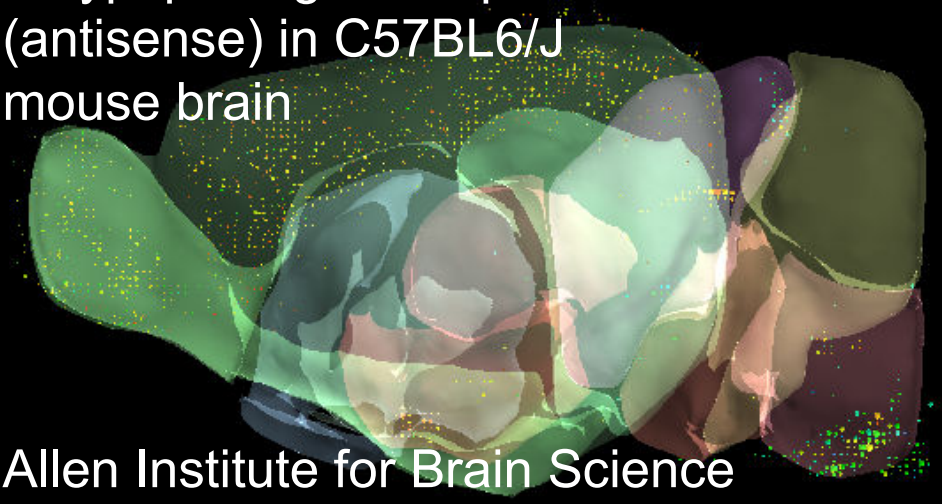
- Background
- Hippocampus
- CCandExtCapsule
- Caudate Putamen
- Anterior Commissure
- Globus Pallidus
- Internal Capsule
- Thalamus
- Cerebellum
- Superior Colliculi
- Ventricles
- Hypothalamus
- Inferior Colliculi
- Central Gray
- Neocortex
- Amygdala
- Olfactory Bulb
- Brain Stem
- RestOfMidbrain
- BasalForebrain Septum
- Fimbria

In vivo



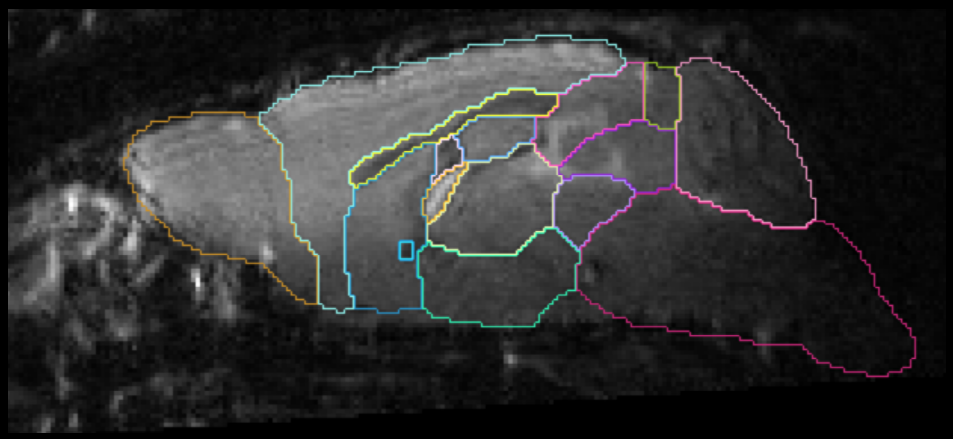
…2007

Vasoactive Intestinal Polypeptide gene expression (antisense) in C57BL6/J mouse brain

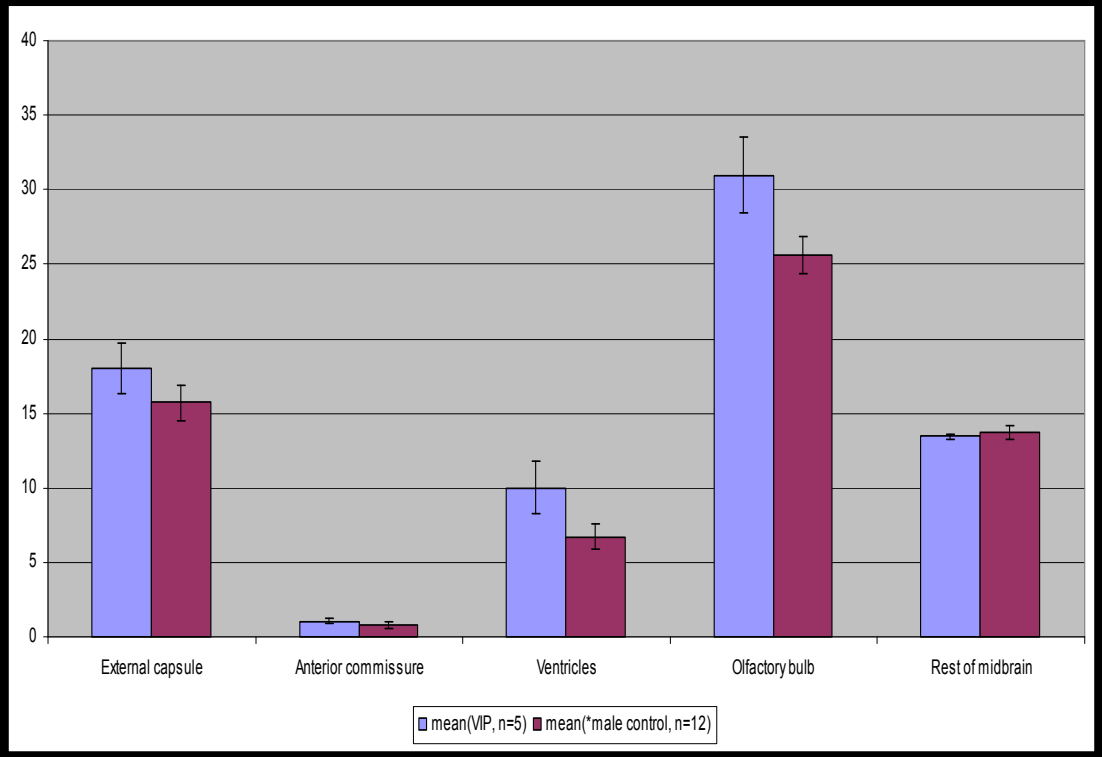


Allen Institute for Brain Science

Gene – expression
+
Brain morphometry



VIP-/- (G_255) In vivo scan, 100 micron^3
Segmented using BNL mouse brain atlas



Benveniste, Ma, Hamilton, Szema, Said, 2007

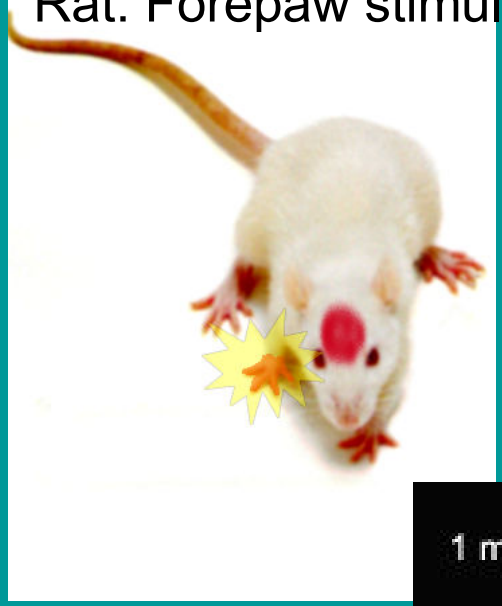
Paramagnetic Effects:

Contrast Materials

fMRI – Two states of Hemoglobin

fMRI: Blood-Oxygen-Level-Dependent signal changes

Rat: Forepaw stimulation, 3Hz

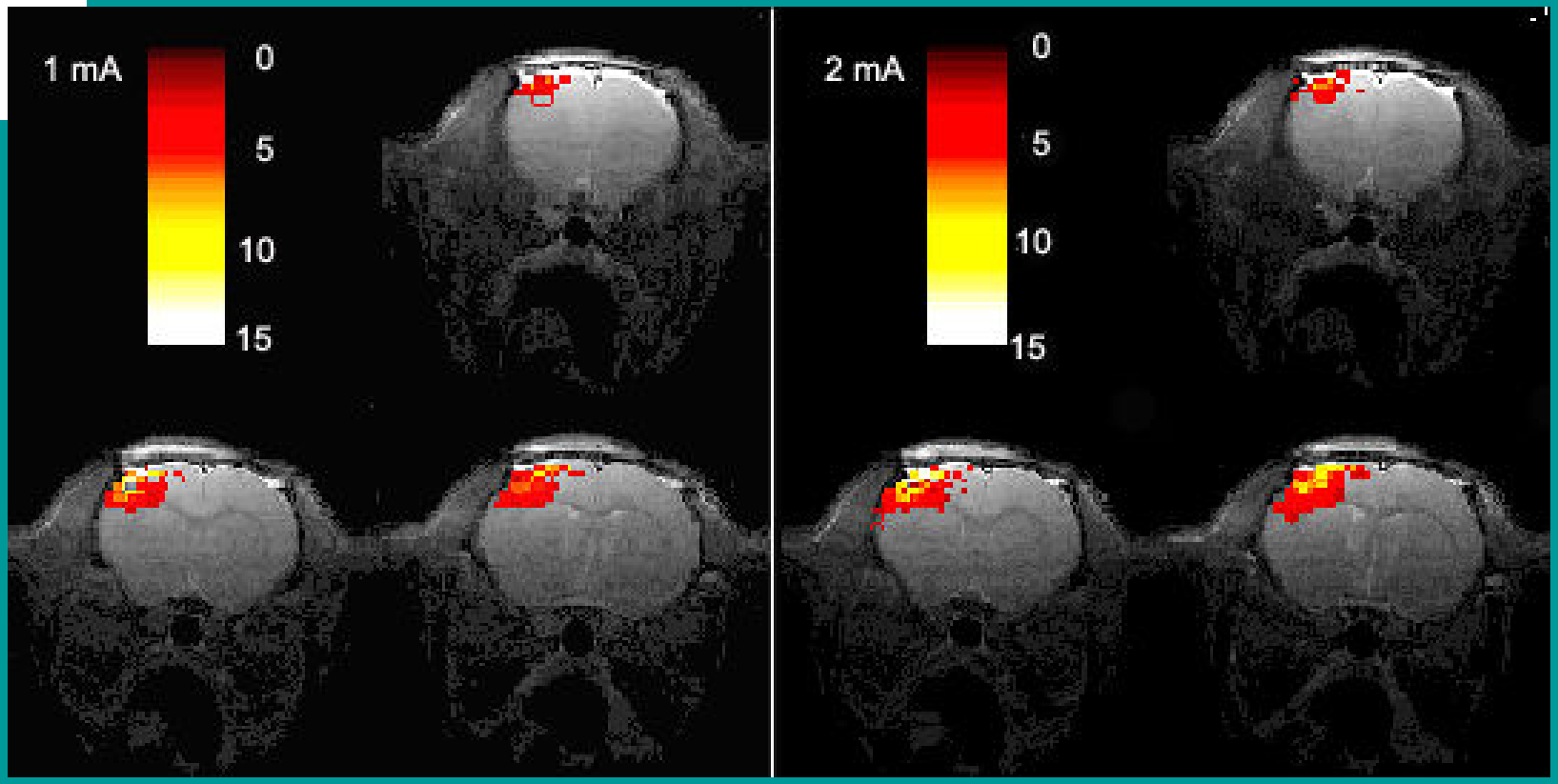


…physiology and anesthesia a big issue!

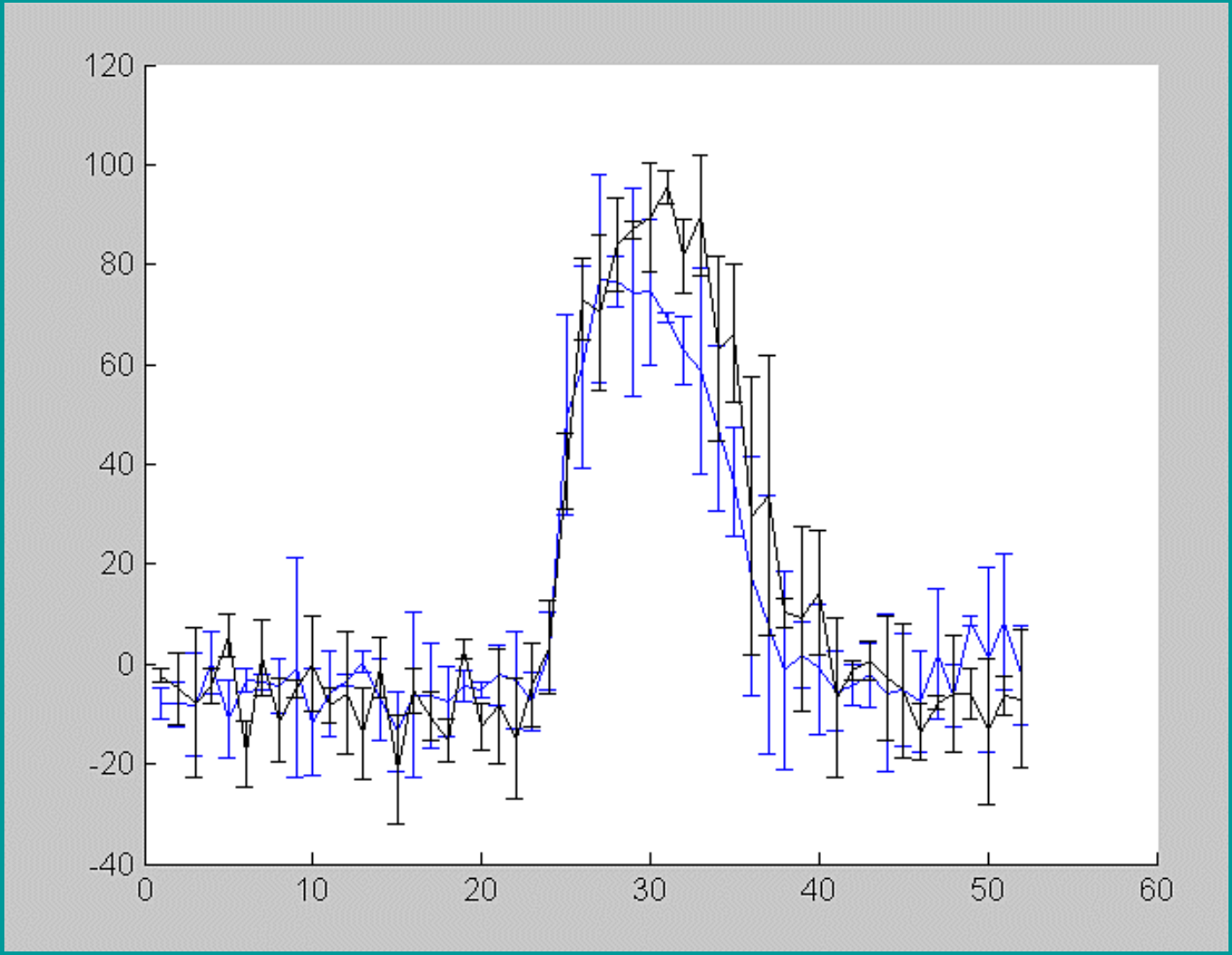
α-chloralose, propofol, dexmedotomidine…isoflurane?

FLASH sequence:

TR=46.875ms
TE=10ms
64x64
3s/image

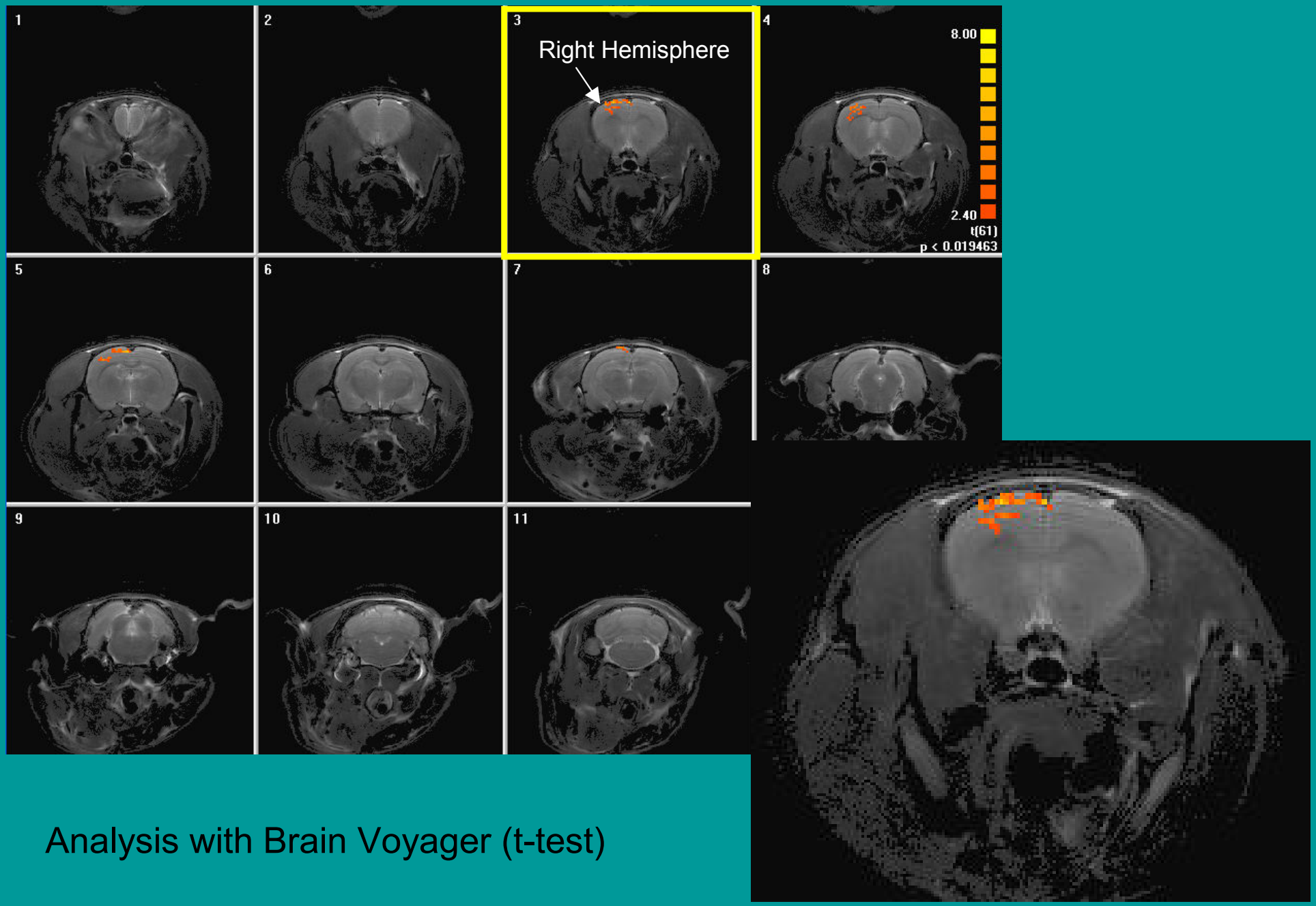


BOLD signal changes



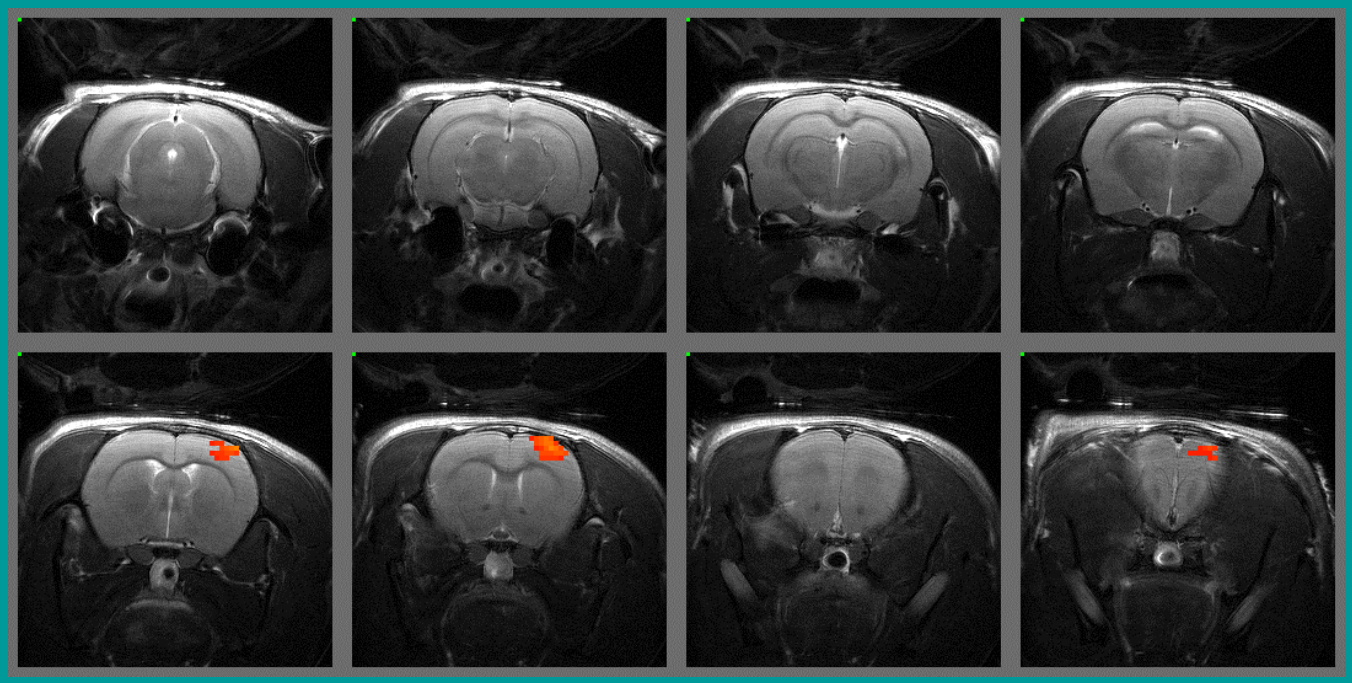
BOLD signal changes with 1mA, 2mA at 3Hz…..

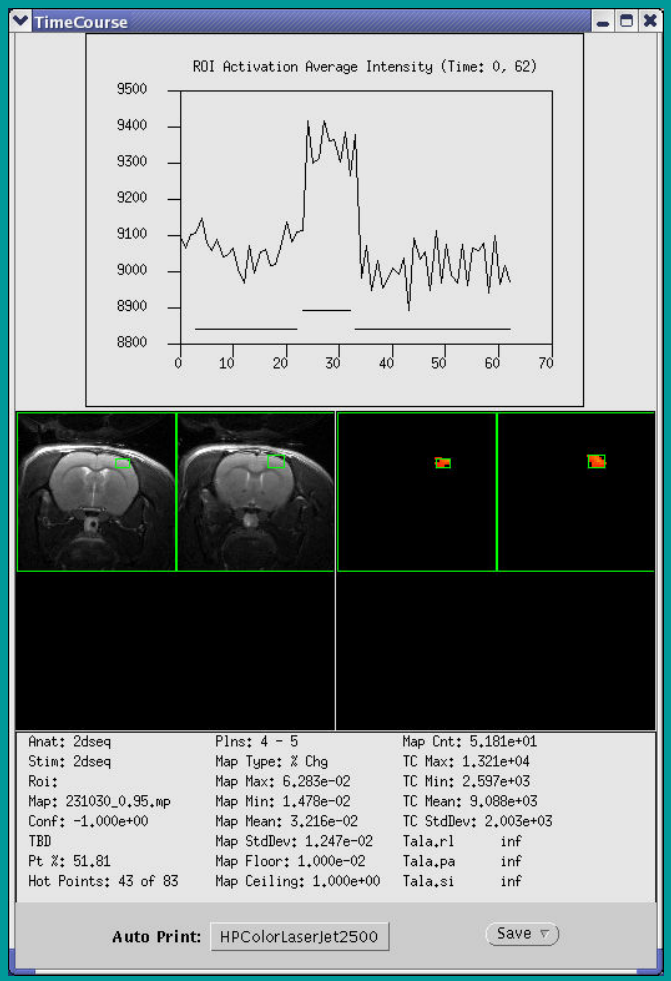
Left Forepaw Stimulation- EPI



Analysis with Brain Voyager (t-test)

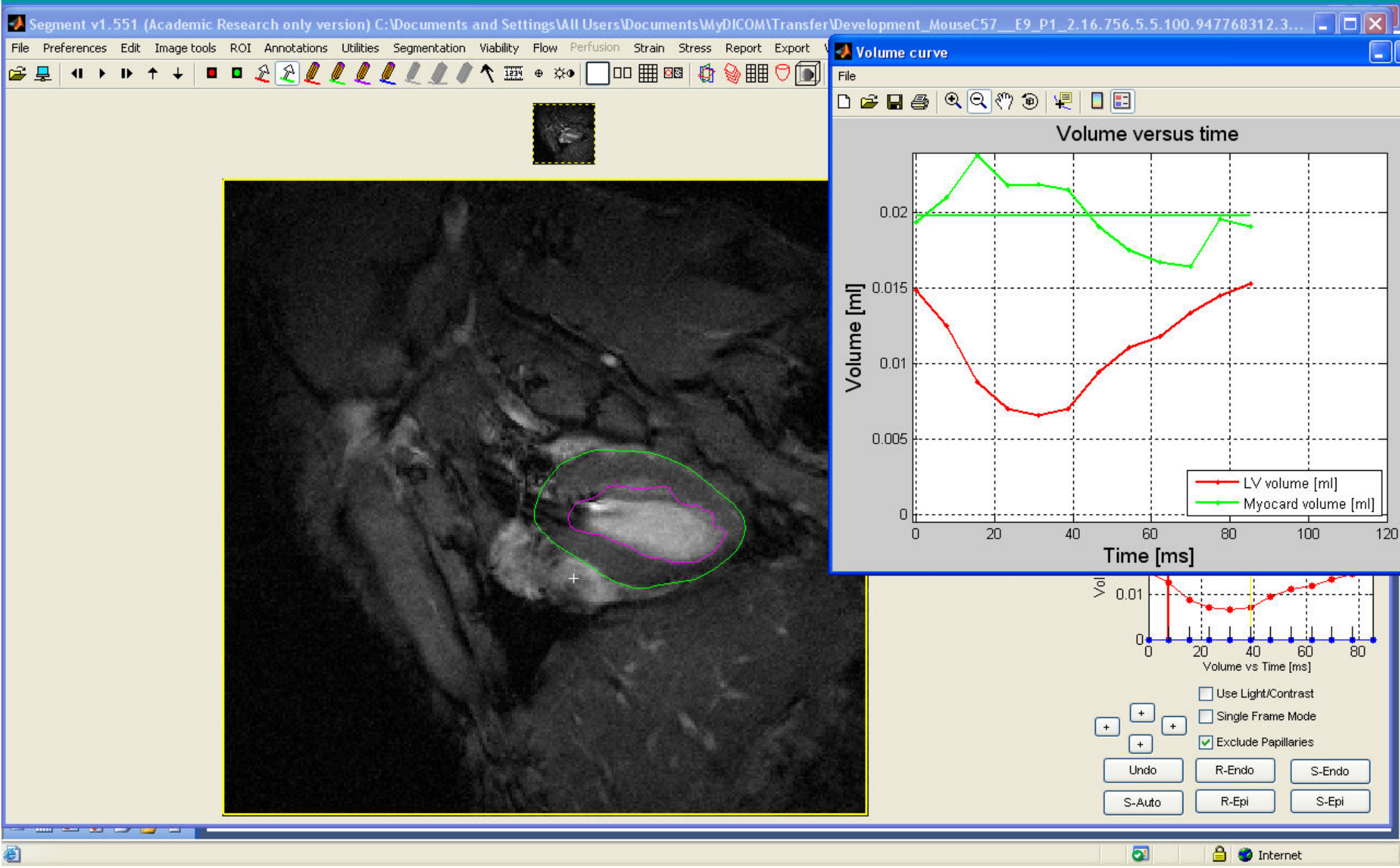
BOLD effect observed in “wild” rat.



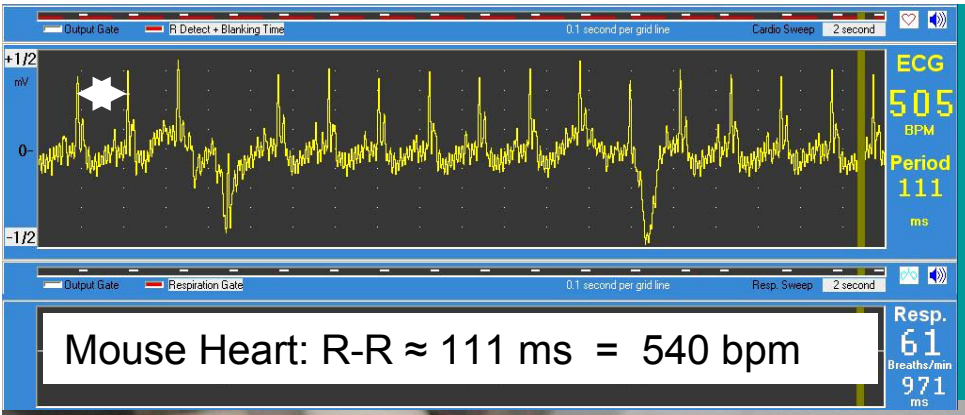


Forepaw stimulation of captured wild rat activates cortical brain area exactly similar to that observed in laboratory bred rats.

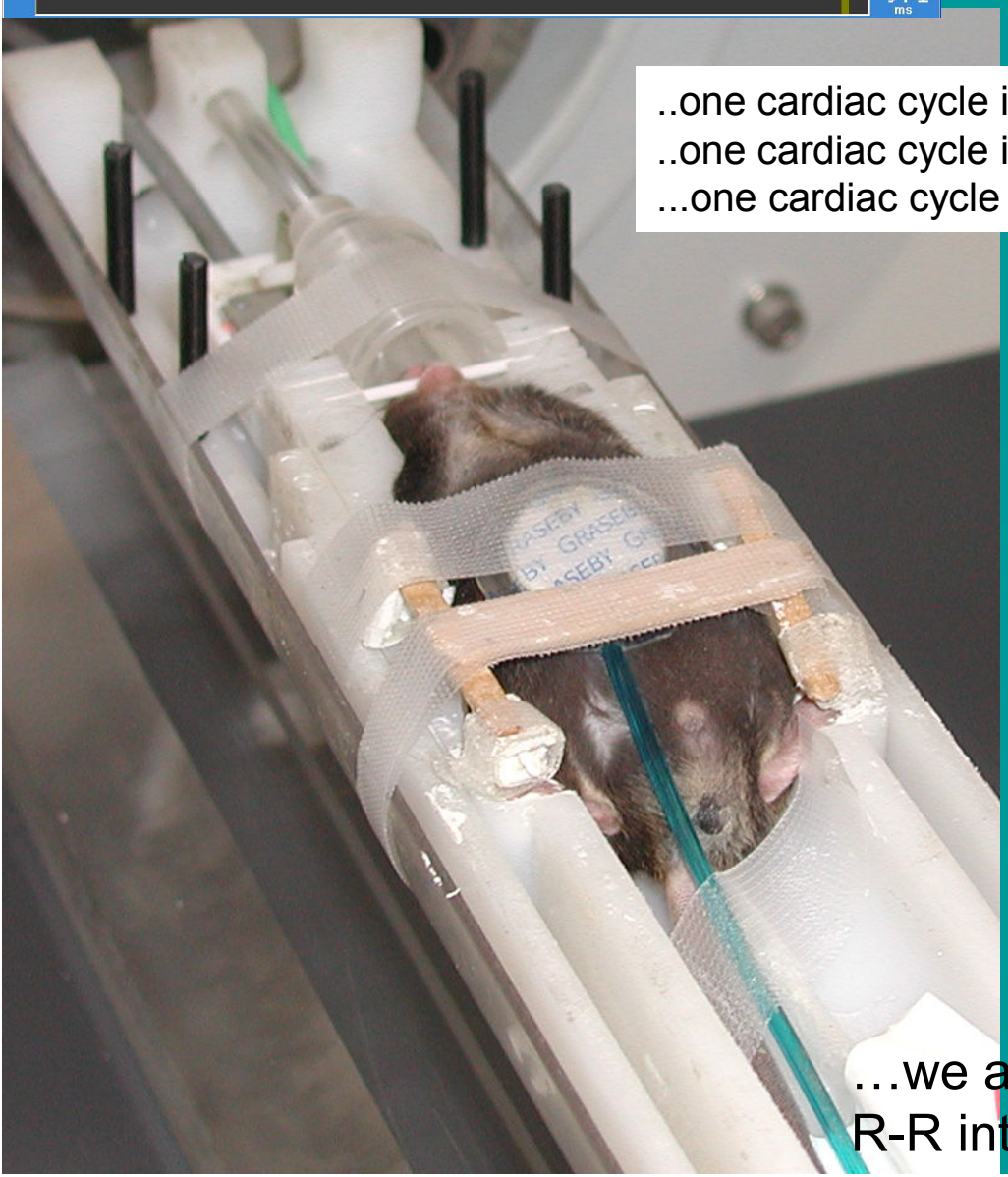
Quantitative Dynamic Measurements



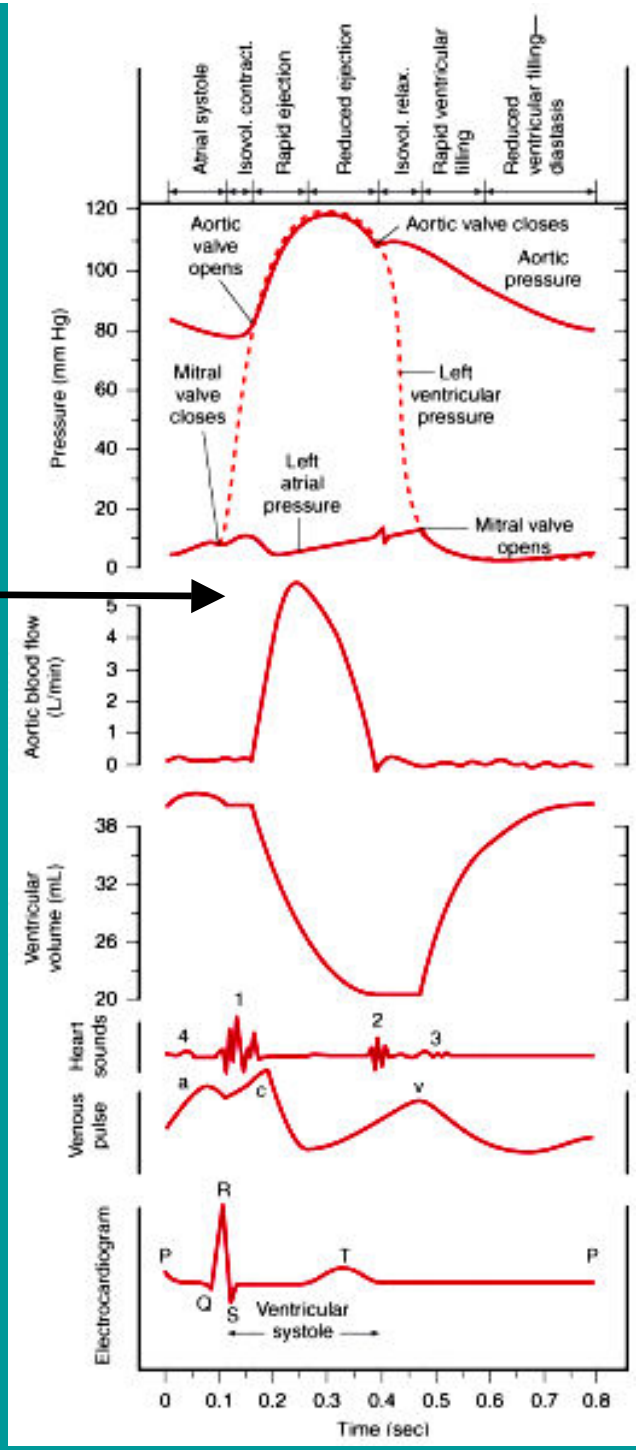
Physiological MR Imaging



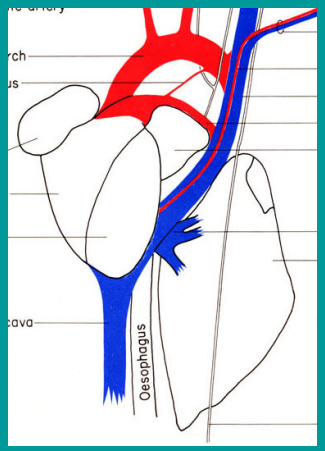
Mouse Heart: R-R ≈ 111 ms = 540 bpm



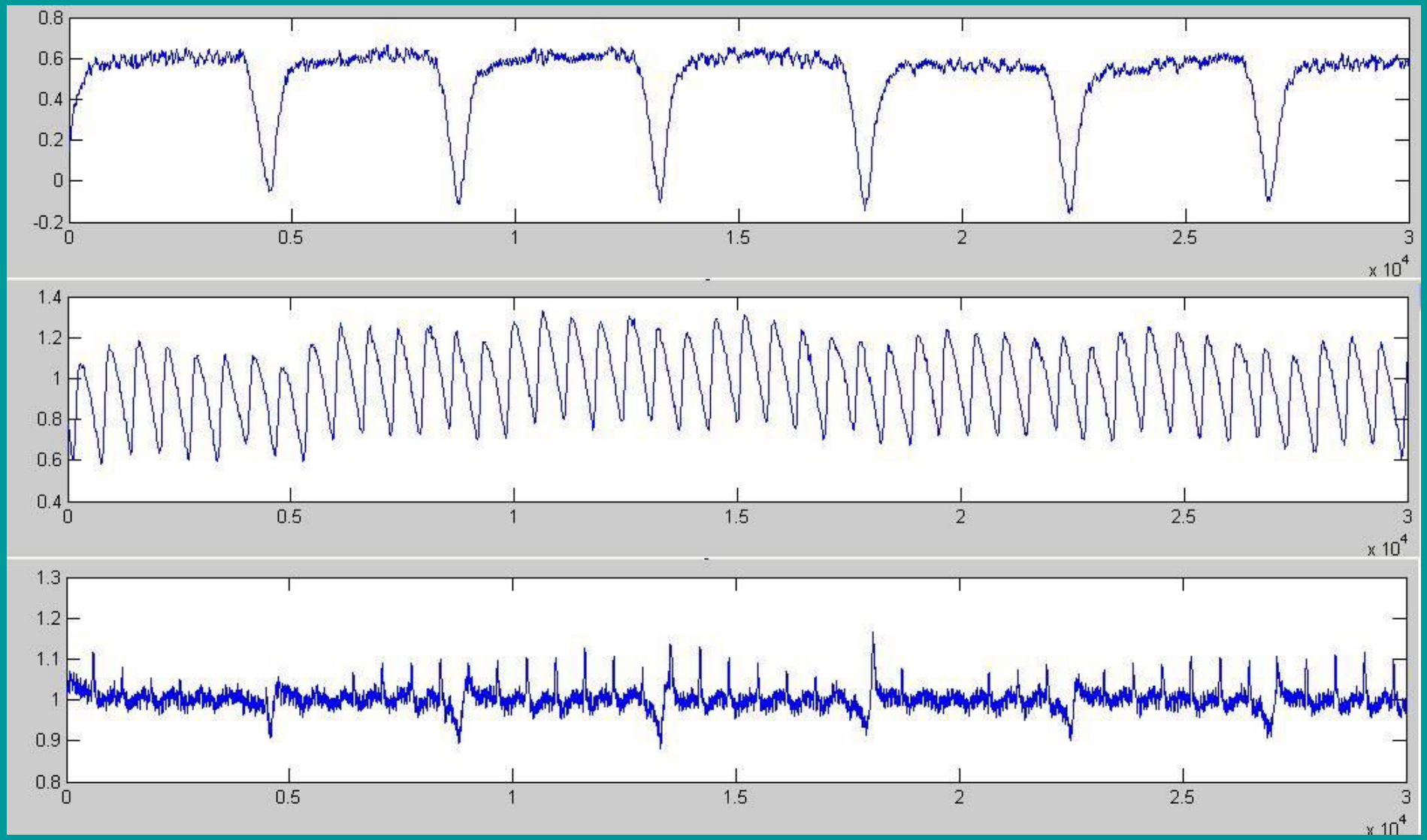
..one cardiac cycle in the mouse ≈ 100ms
..one cardiac cycle in the rat ≈ 180-200ms
...one cardiac cycle in human ≈ 800ms



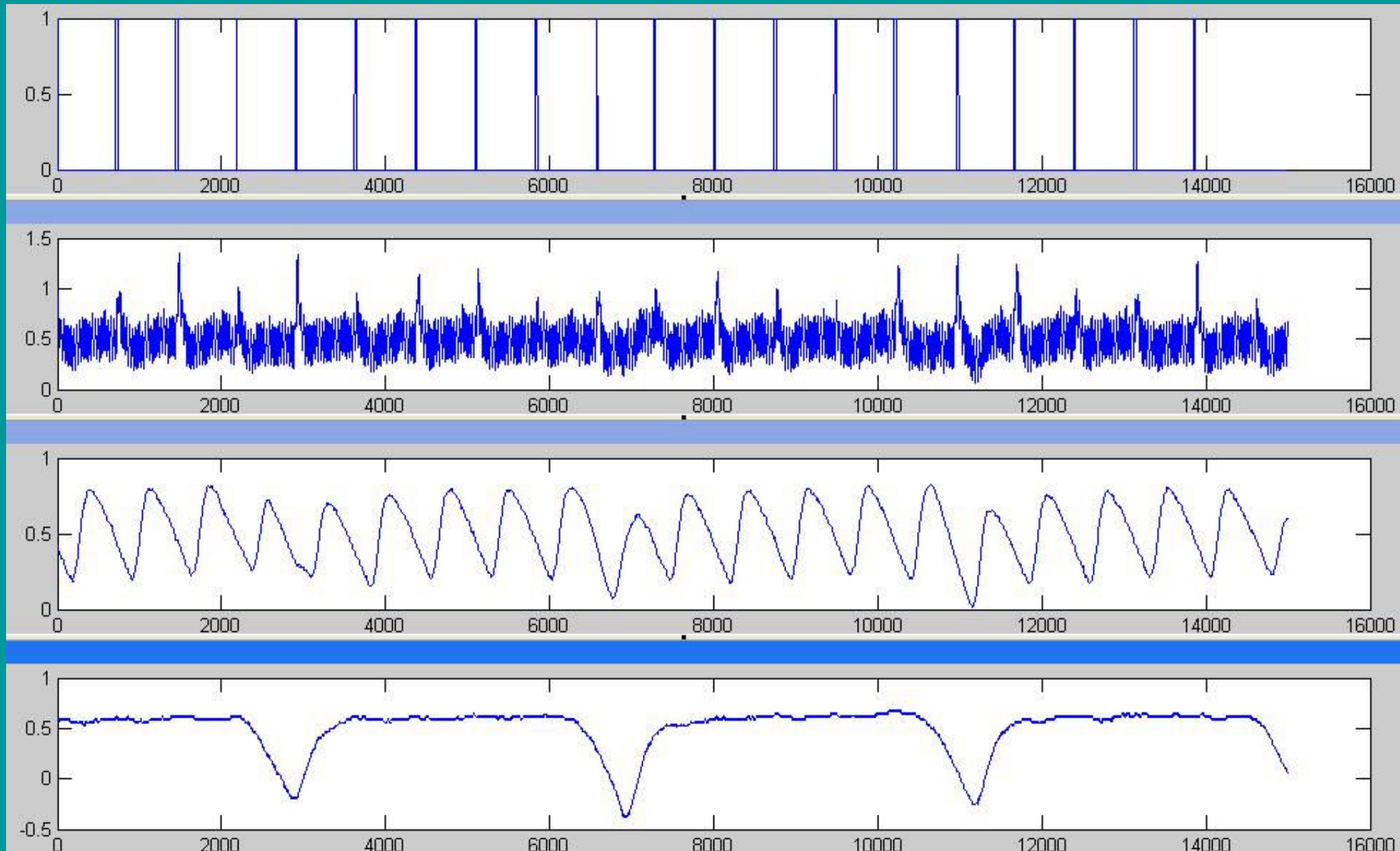
Mouse Heart



…we are setting the repetition time lower that the R-R interval ….*prospective* gating…

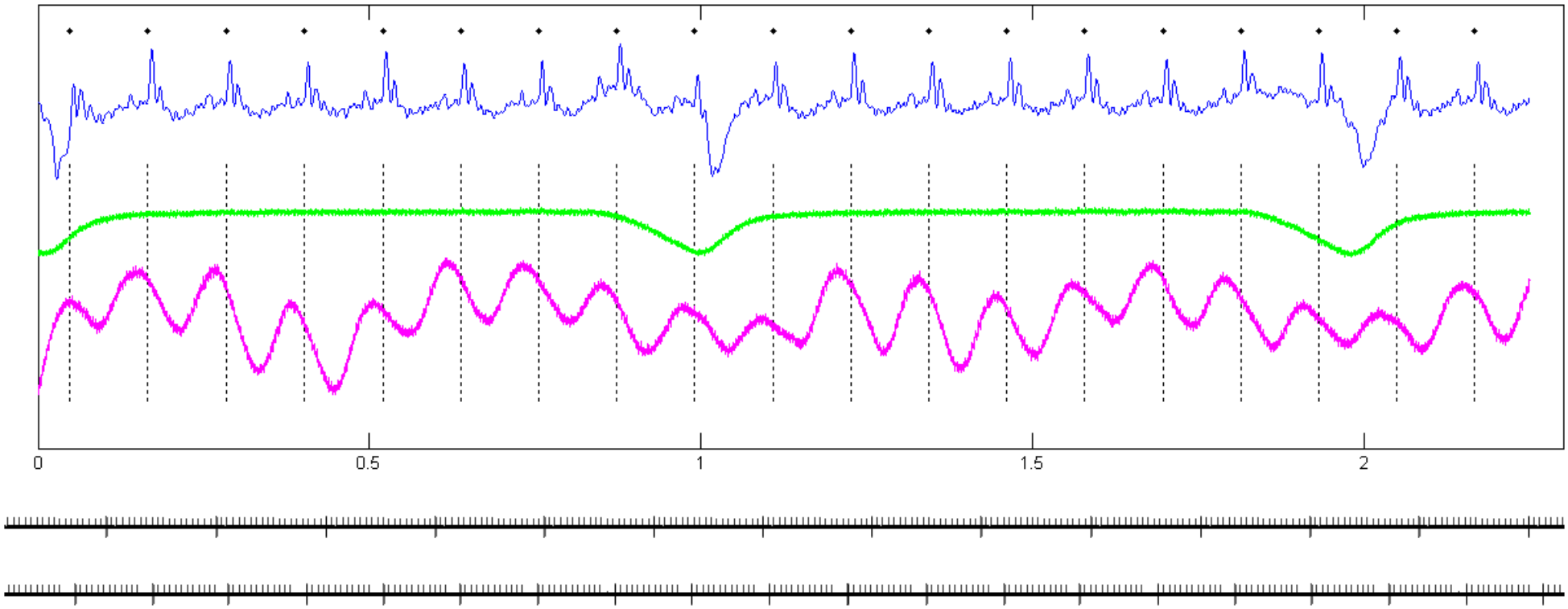


Example of raw capture waveforms



Second example showing capture of output SAI triggers

Prospective or Retrospective Gating modes

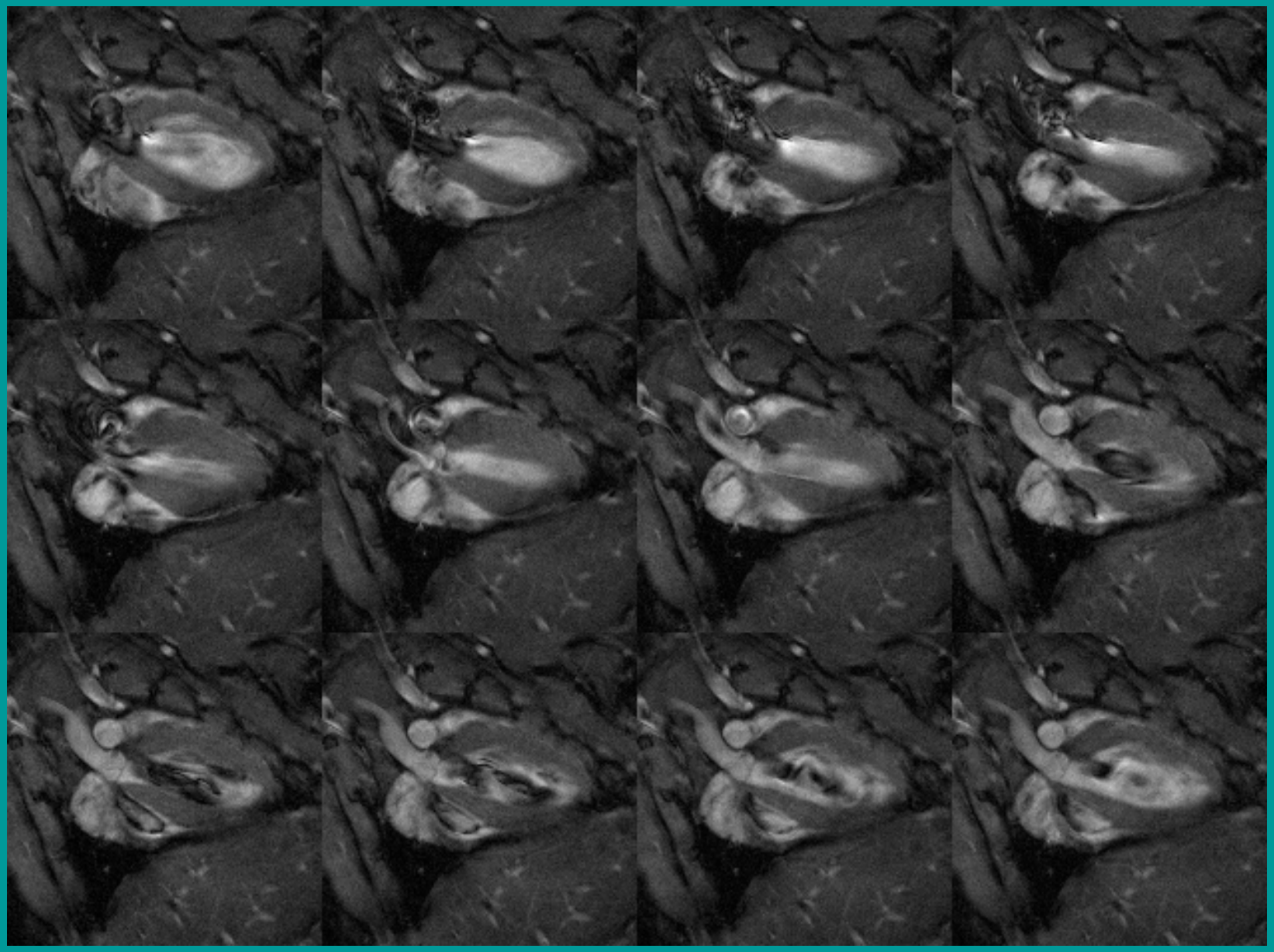


Tick marks demonstrate timing relationship of MRI signal acquisition to captured waveforms for two cases:

Top line shows continuous acquisition

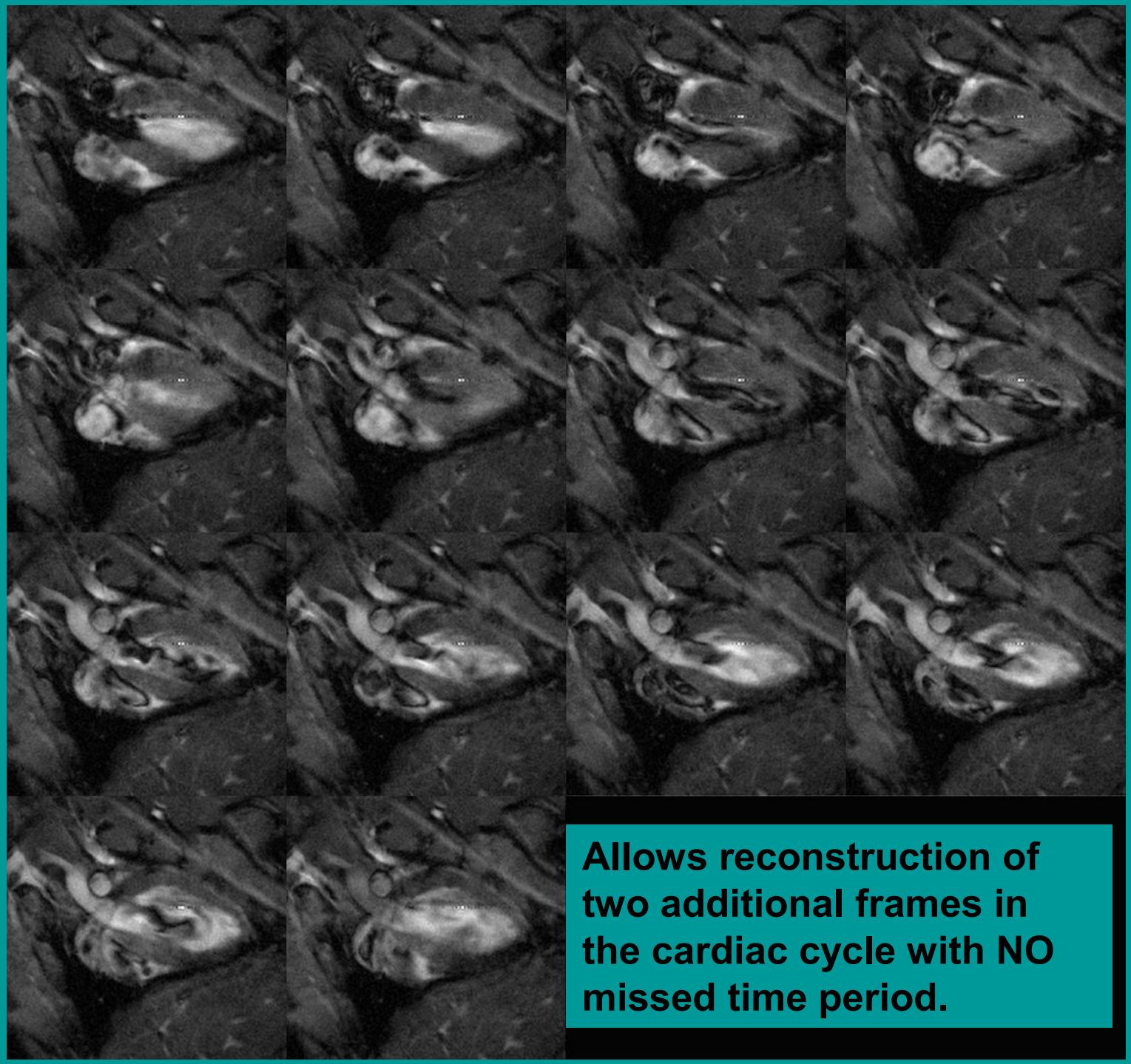
Lower set of shows timing for triggered acquisition

Triggered MRI acquisition of CINE images



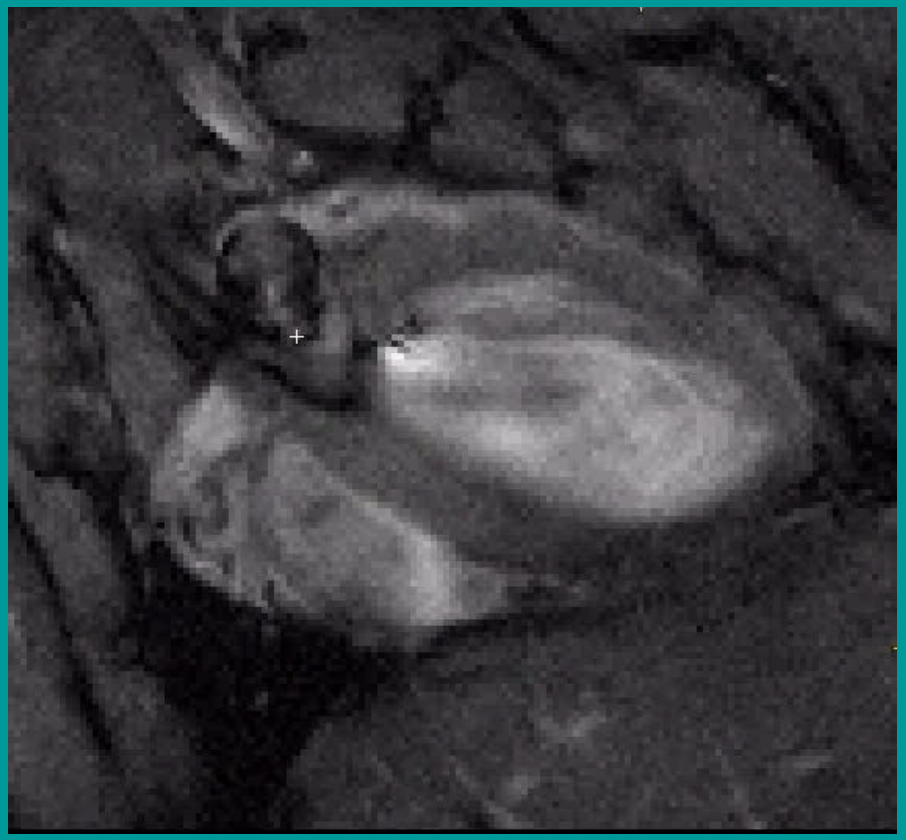
Triggered Acquisition allows 12 frames in Cardiac cycle

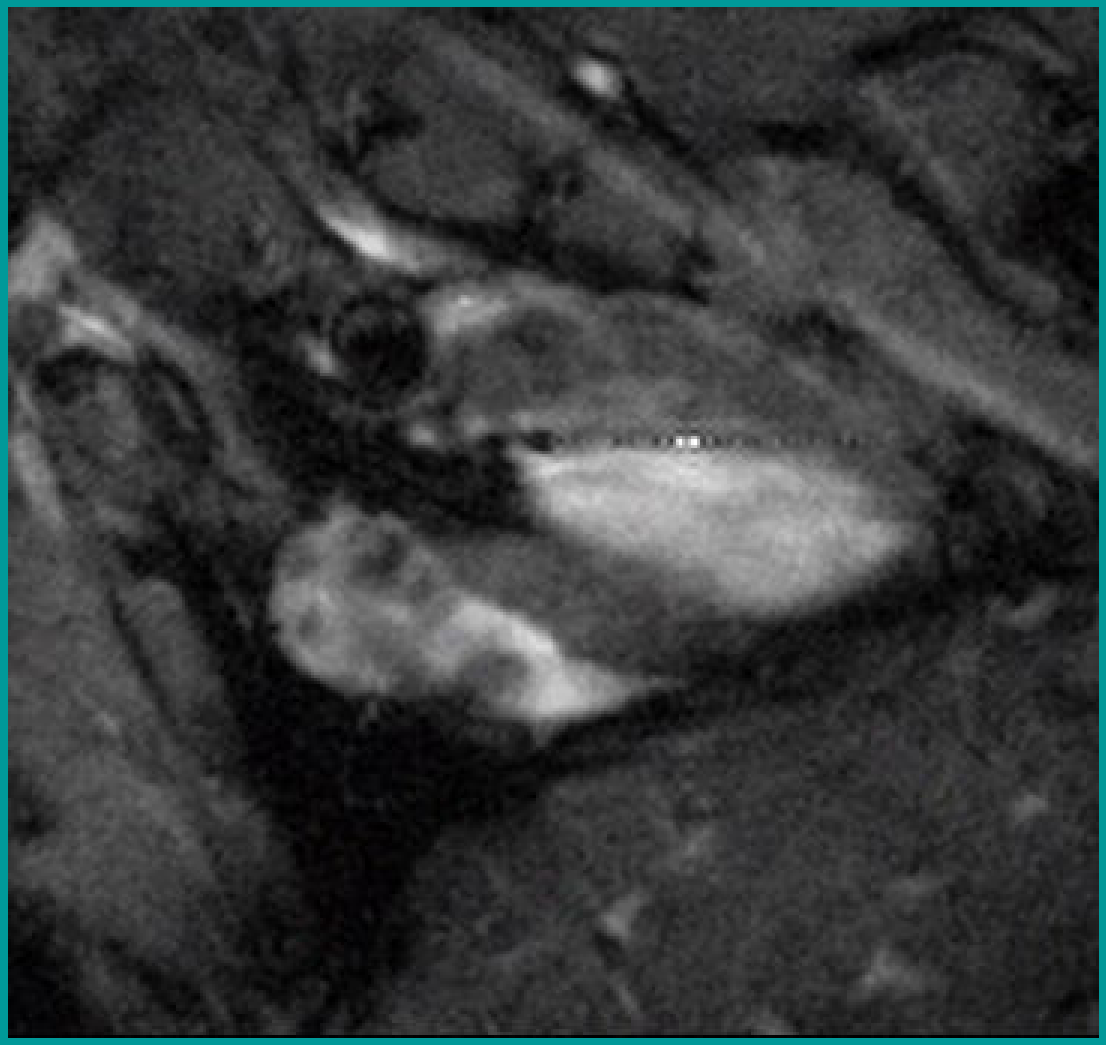
Continuous Acquisition with post acquisition reordering



Allows reconstruction of two additional frames in the cardiac cycle with NO missed time period.

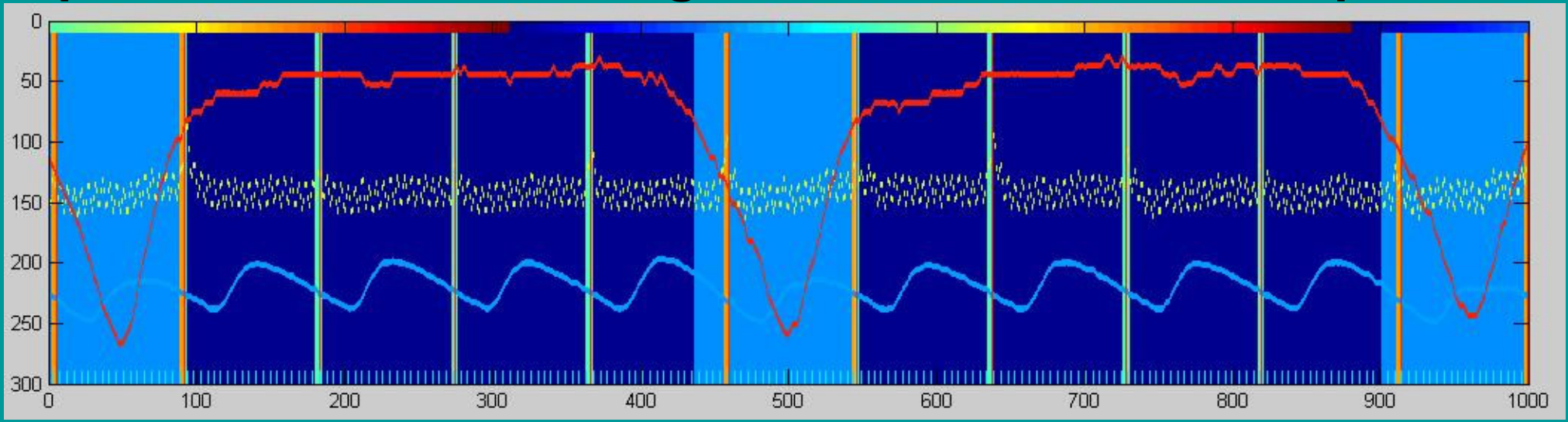
Prospective vs Retrospective



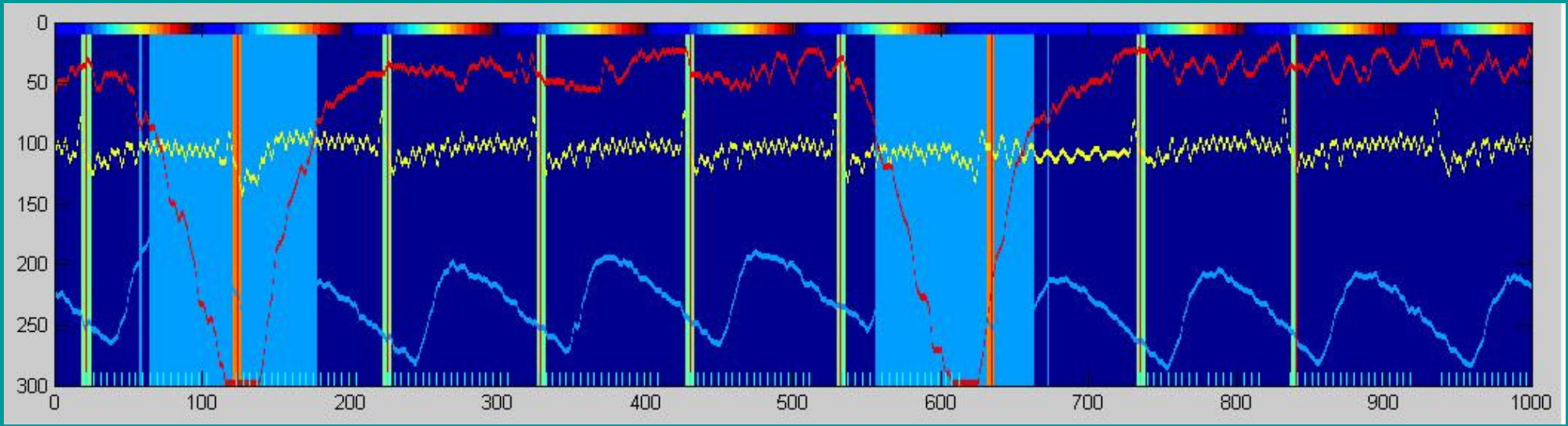


Comparision of images reconstructed from triggered and continuously acquired MRI data

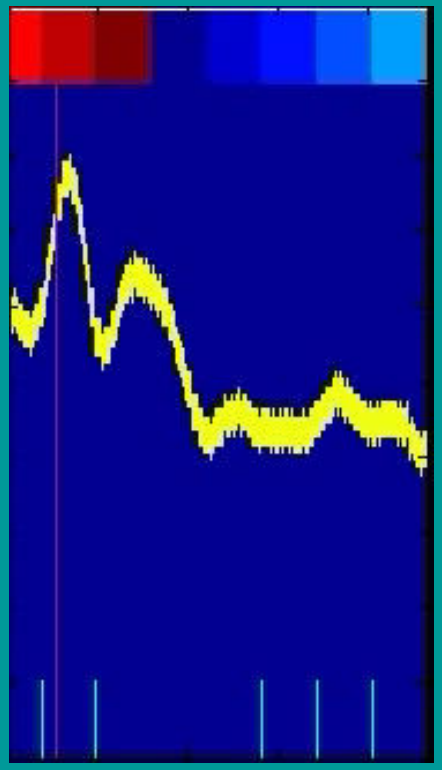
Spectral scale shows single Phase Encode level repetitions



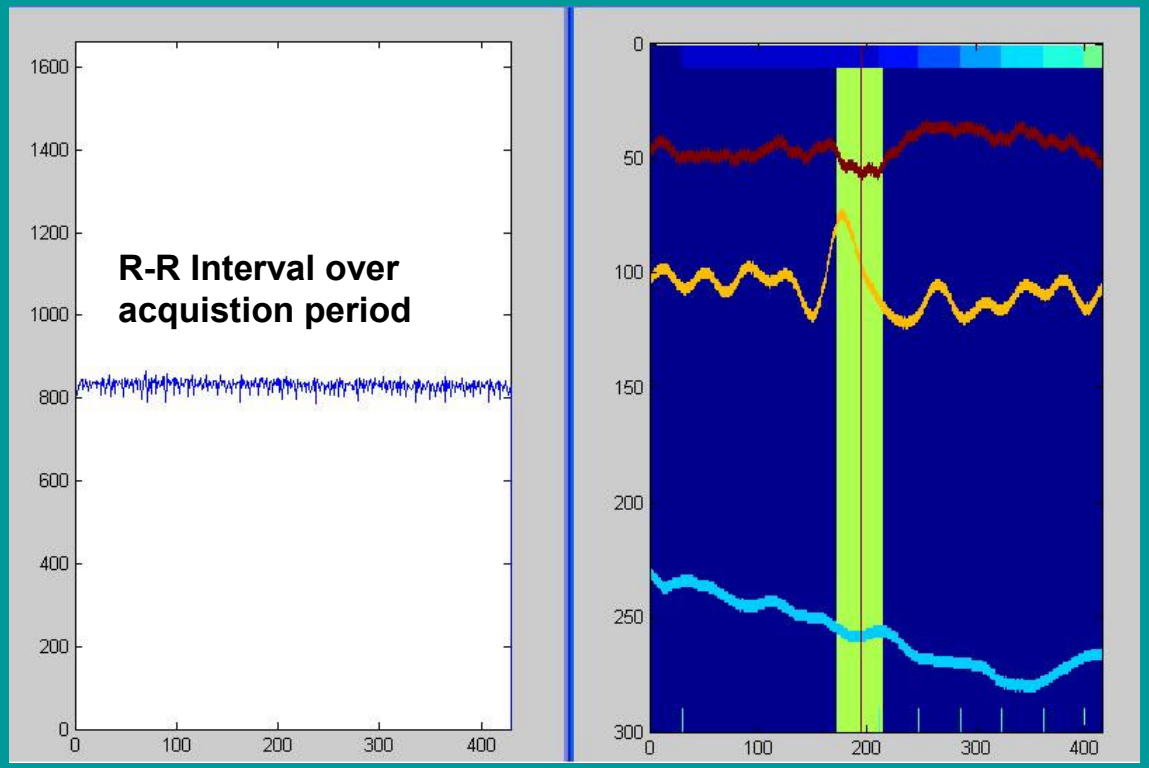
Top strip show continuous acquisition with MRI signal timing shown by tick marks at bottom.



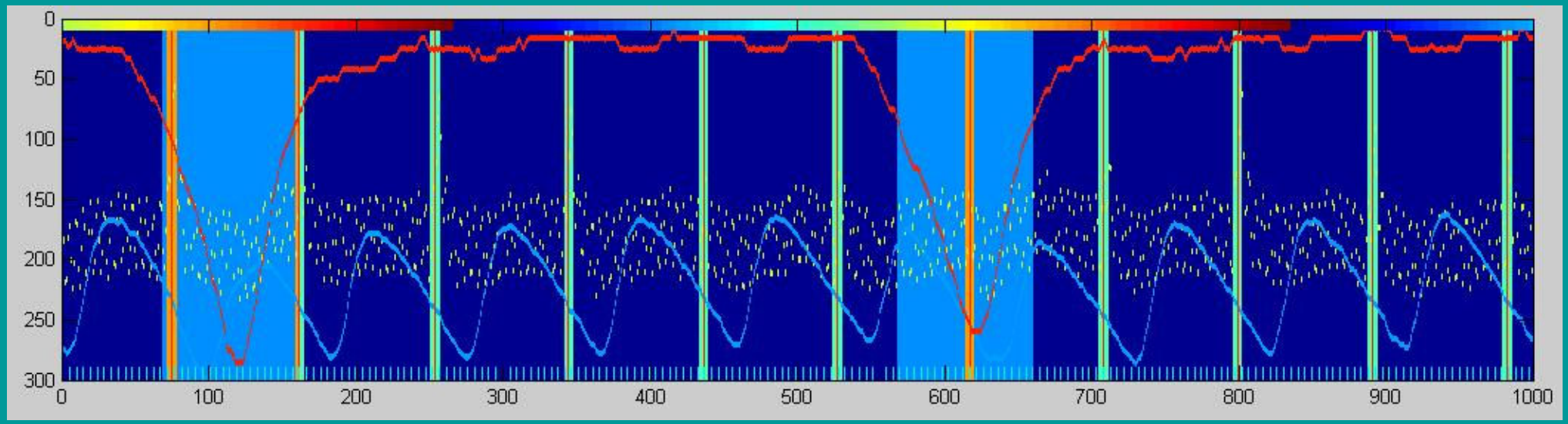
Lower example is for triggered acquisition. Note timing gaps in tick marks.

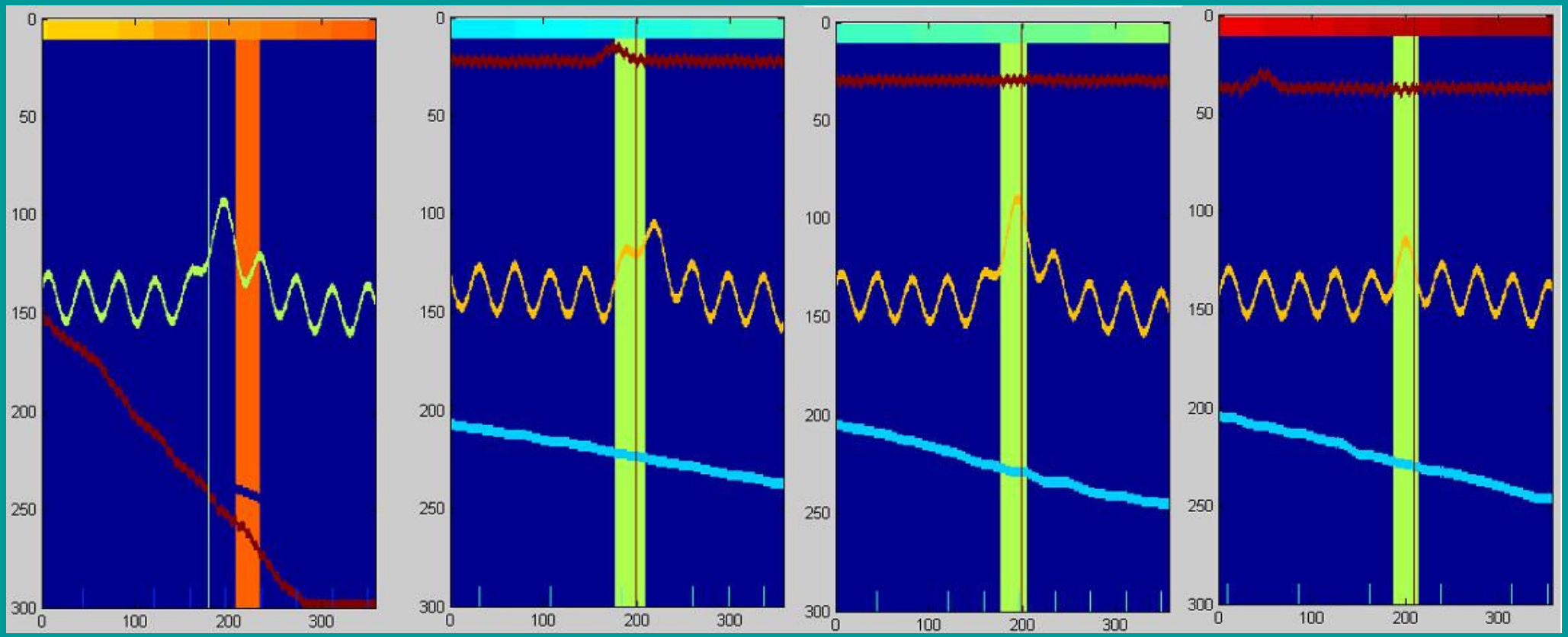


Triggered on
previous R wave



Demonstration of ECG timing stability wrt previous R wave

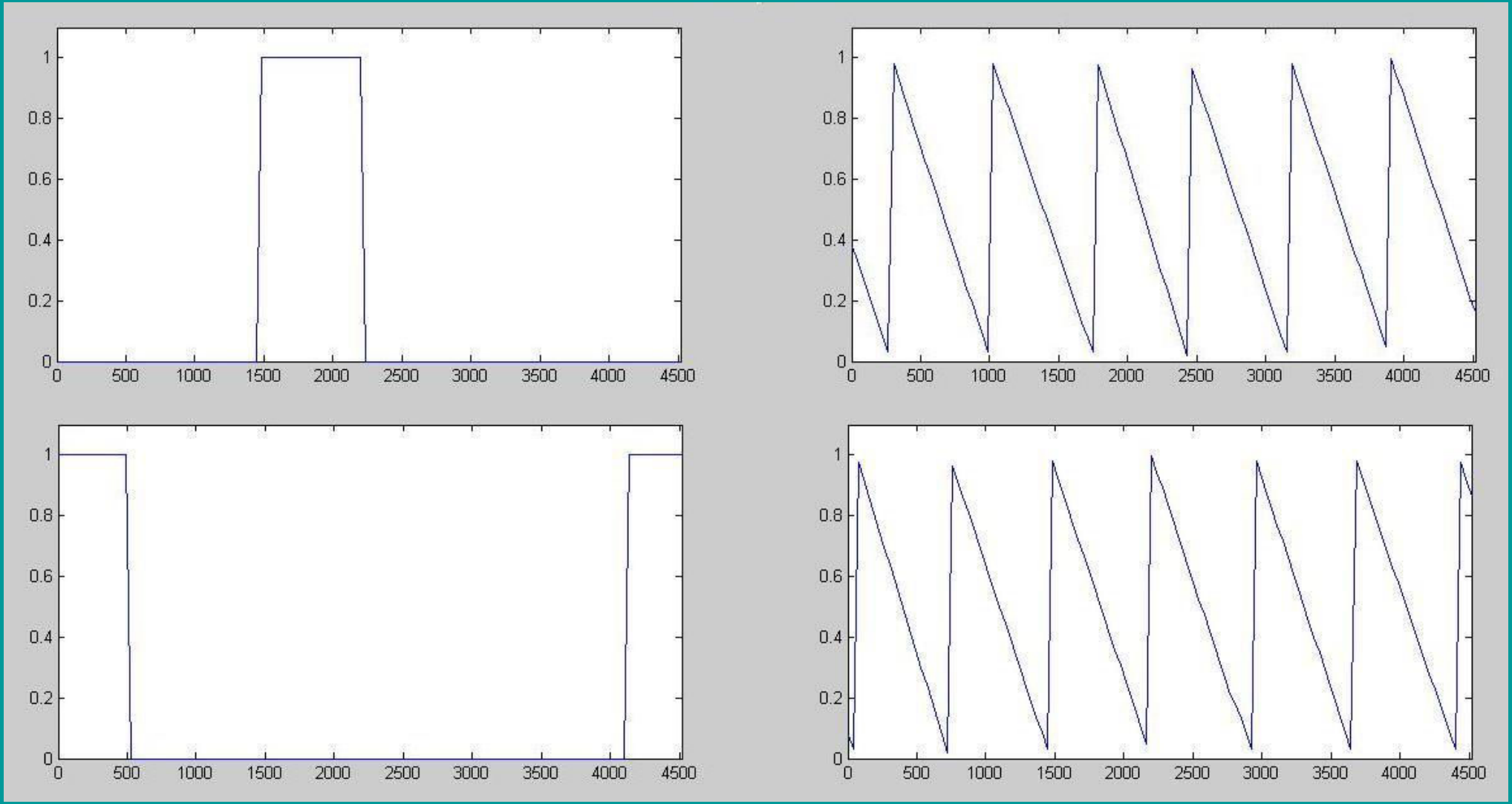




Snapshots compare timings derived separately from ECG and Pulse waveforms.

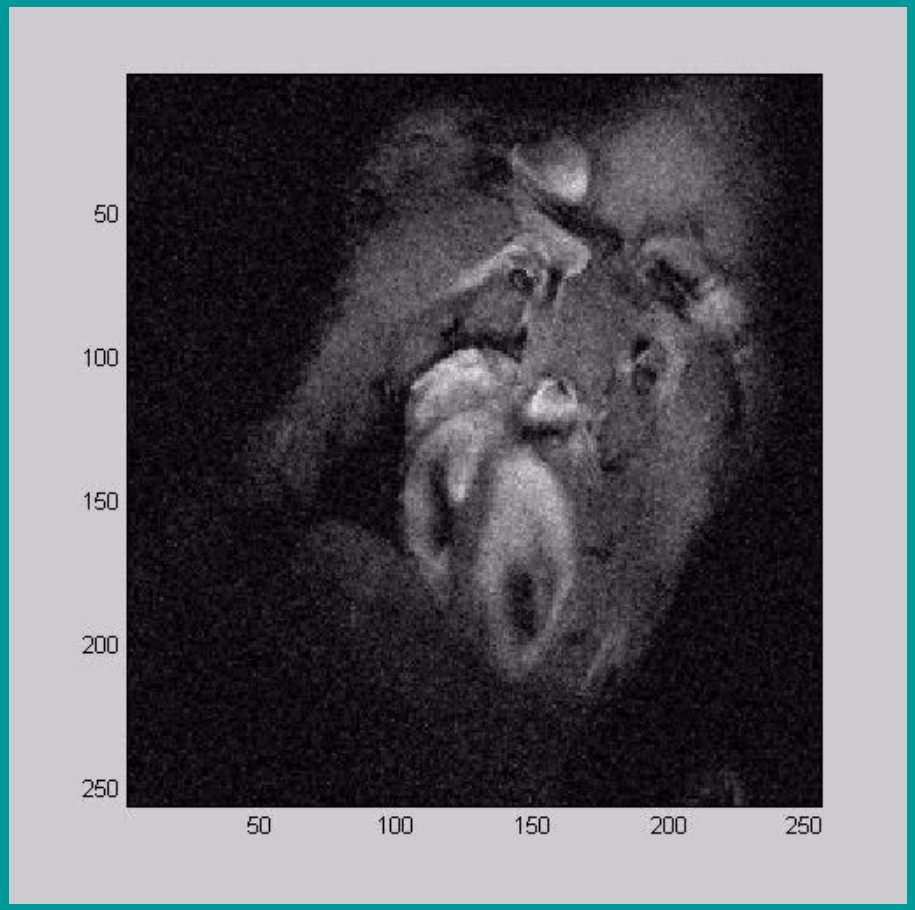
The first panel shows the effect of respiration on timing.

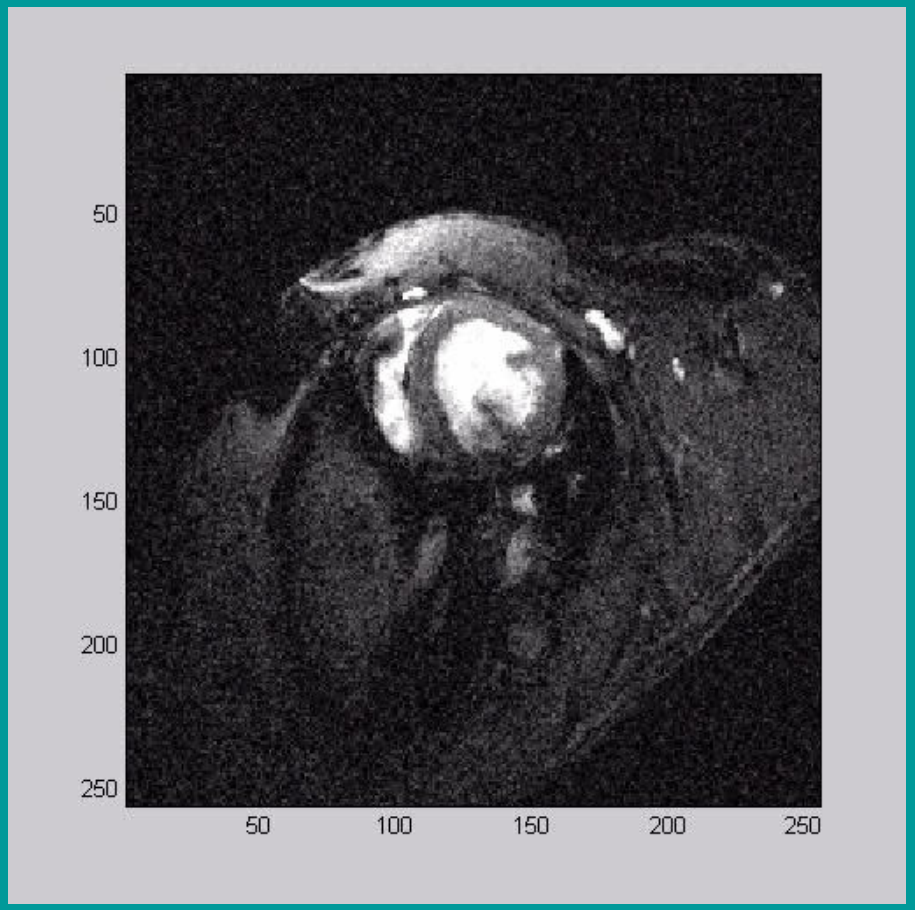
MR acquisitions before (top) and after (lower) reordering



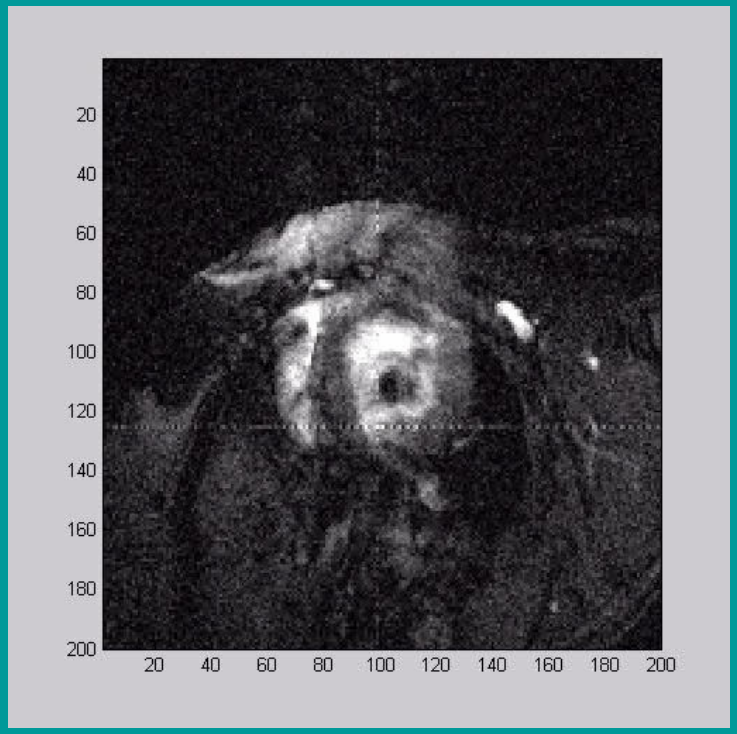
Sawtooth represents R-R interval phasing of acquired MRI data timings.

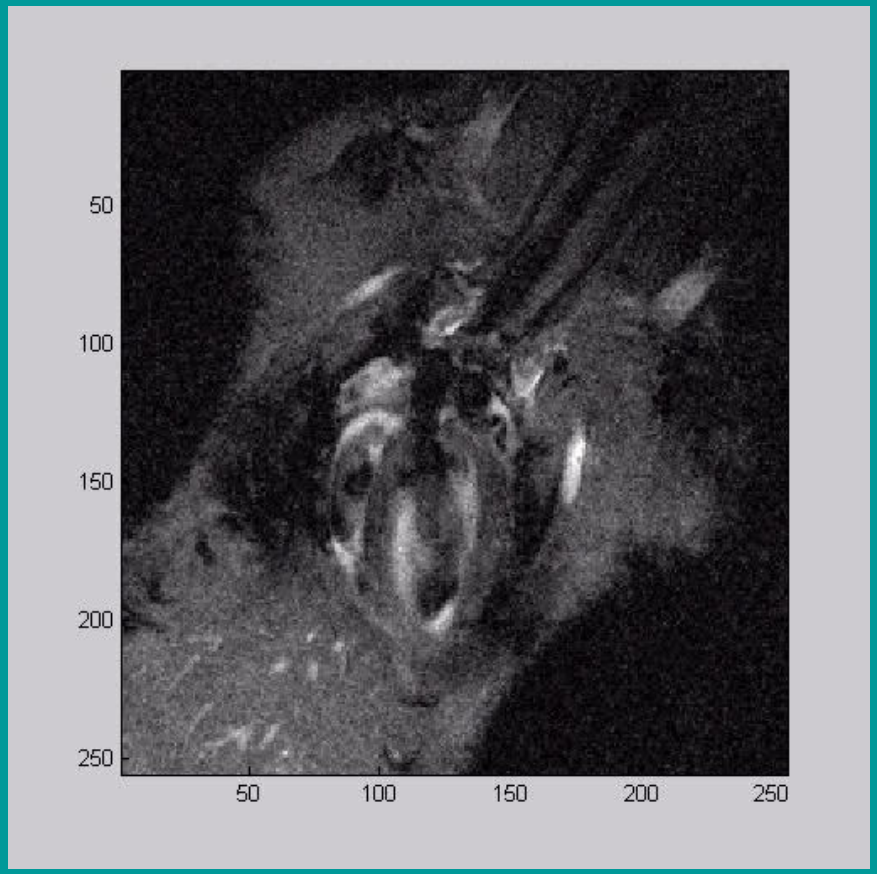
Plots on left show position of Respiration Gate.

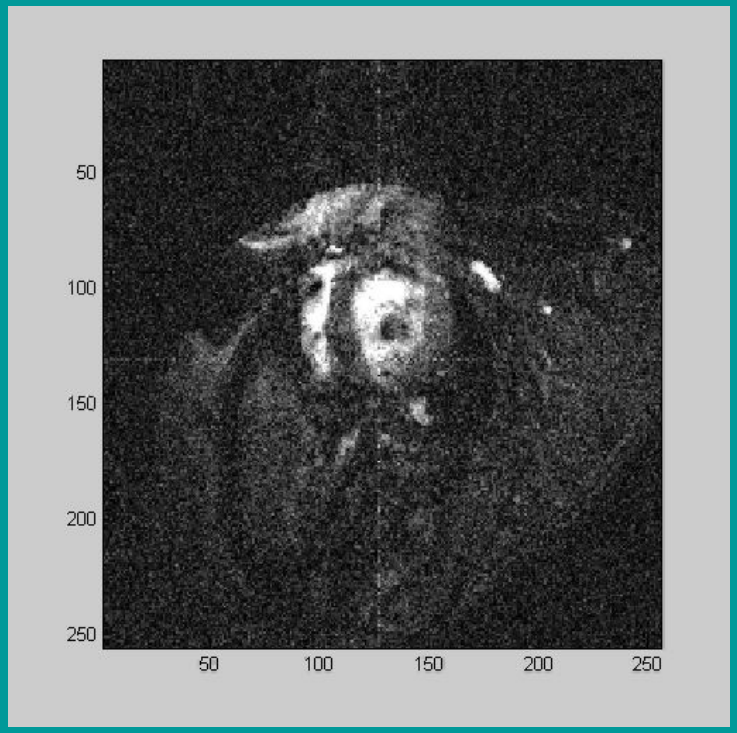




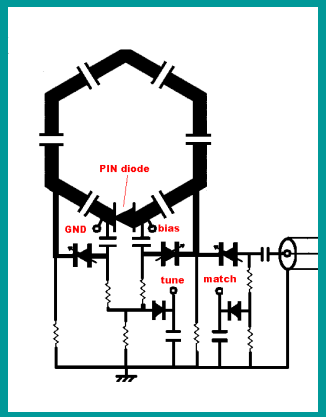
Prospectively gated CINE images

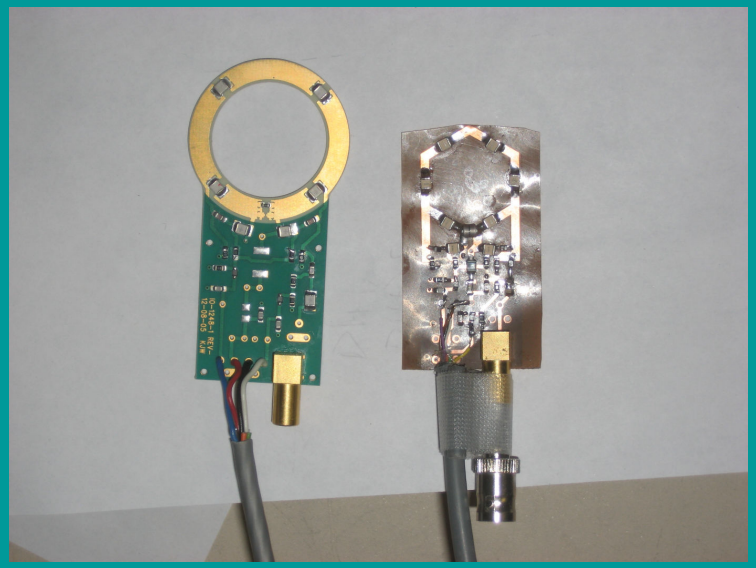


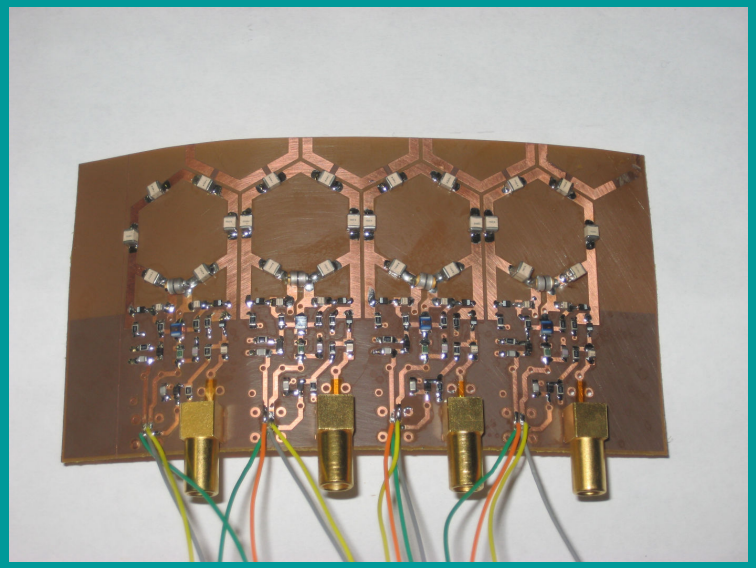


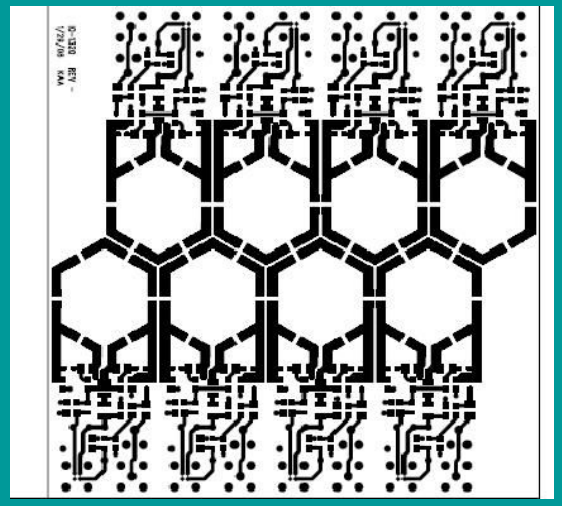


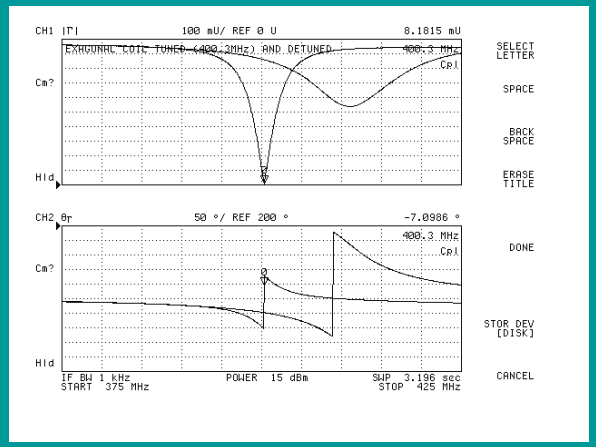
Retrospectively ordered CINE images with various Respiration Strategies

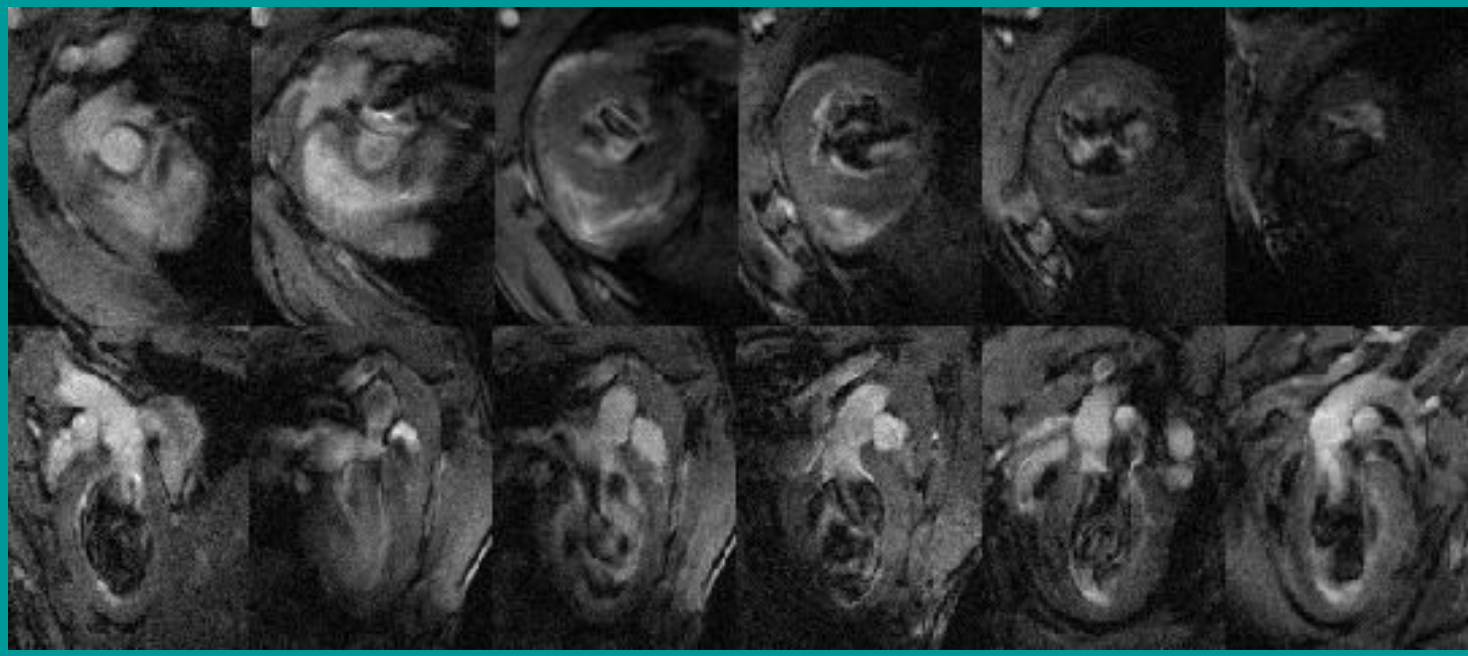

PIN diode
GND
bias
tune
match

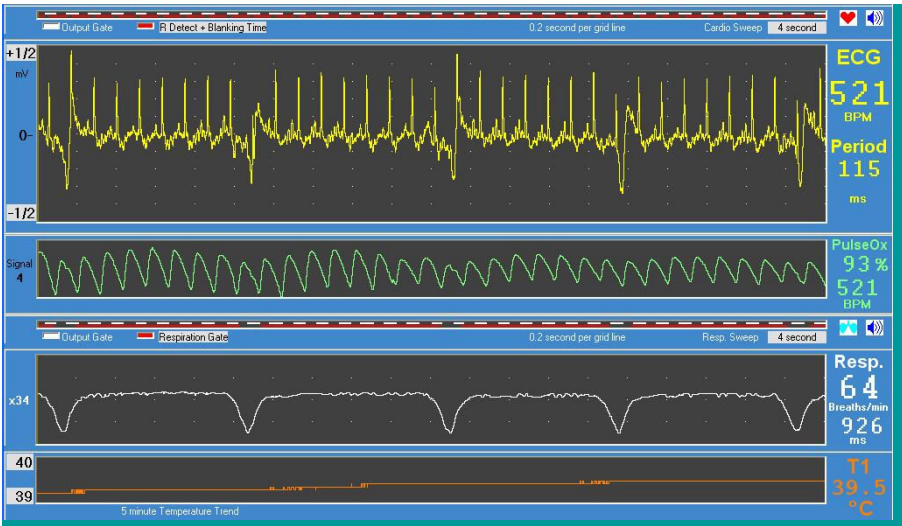


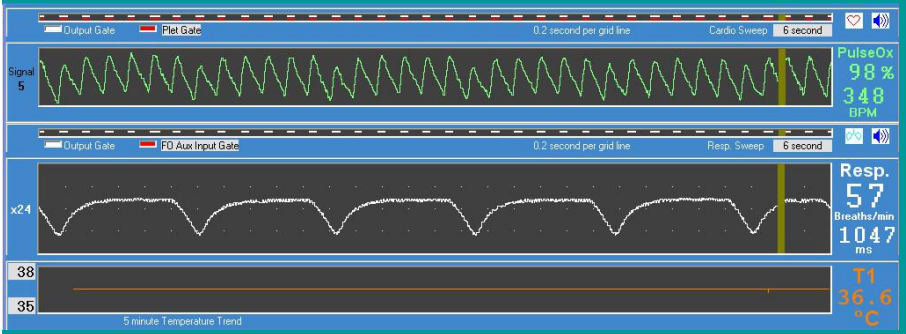




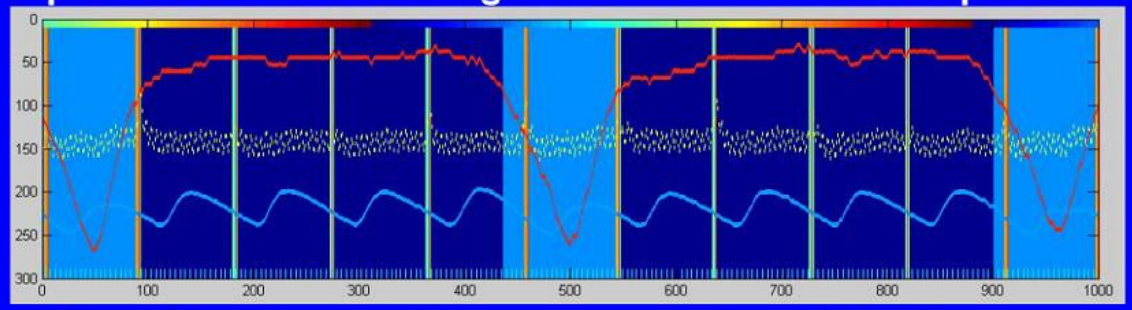

CH1 |Γ| 100 mU/ REF 0 U 8.1815 mU
EXAGONAL COIL TUNED (400.3MHz) AND DETUNED
400.3 MHz
Cpl
Cm?
Hld
CH2 θr 50 °/ REF 200 ° -7.0986 °
400.3 MHz
Cpl
Cm?
Hld
IF BW 1 kHz
POWER 15 dBm
SWP 3.196 sec
START 375 MHz
STOP 425 MHz
SELECT LETTER
SPACE
BACK SPACE
ERASE TITLE
DONE
STOR DEV [DISK]
CANCEL



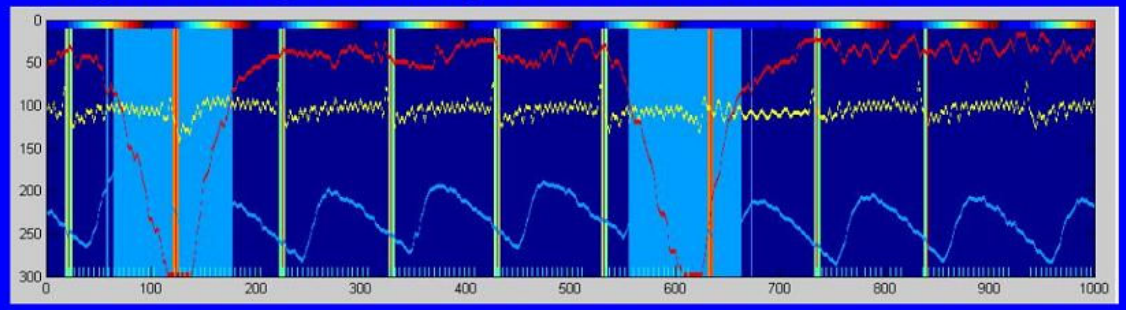




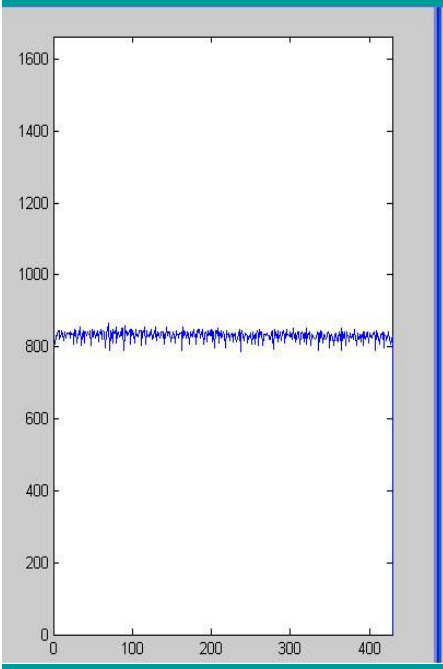
Spectral scale shows single Phase Encode level repetitions

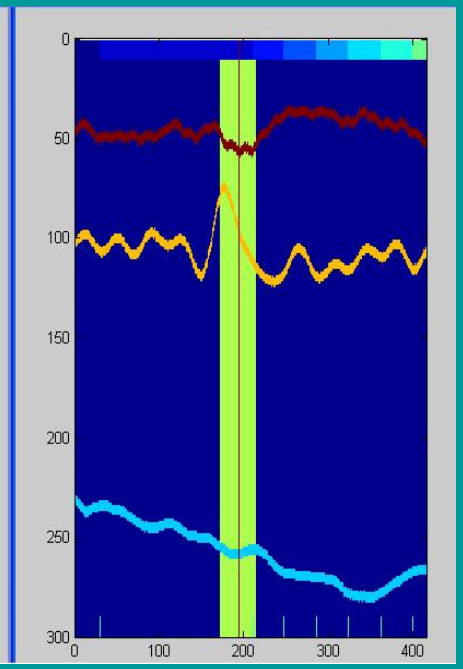


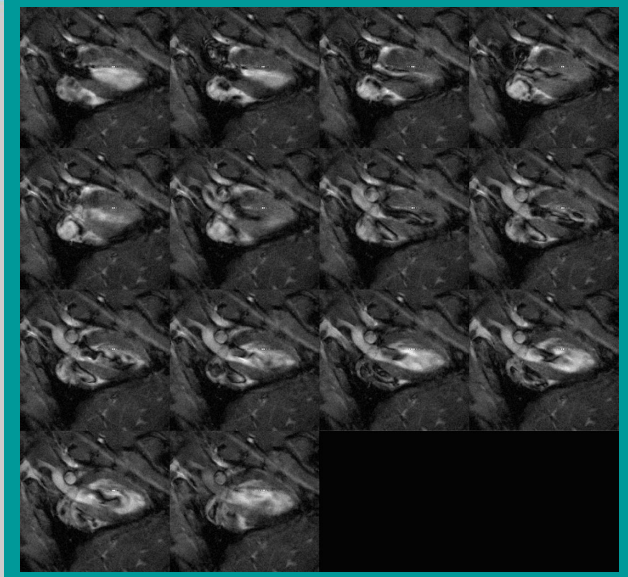
Top strip show continuous acquisition with MRI signal timing shown by tick marks at bottom.

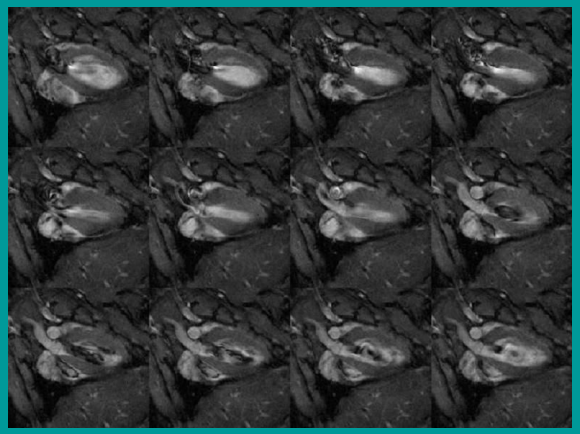


Lower example is for triggered acquisition. Note timing gaps in tick marks.

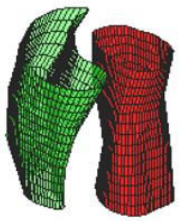


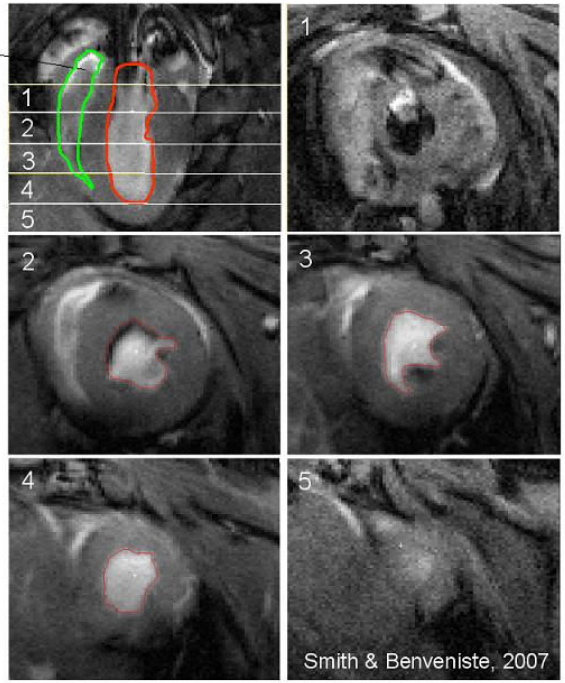




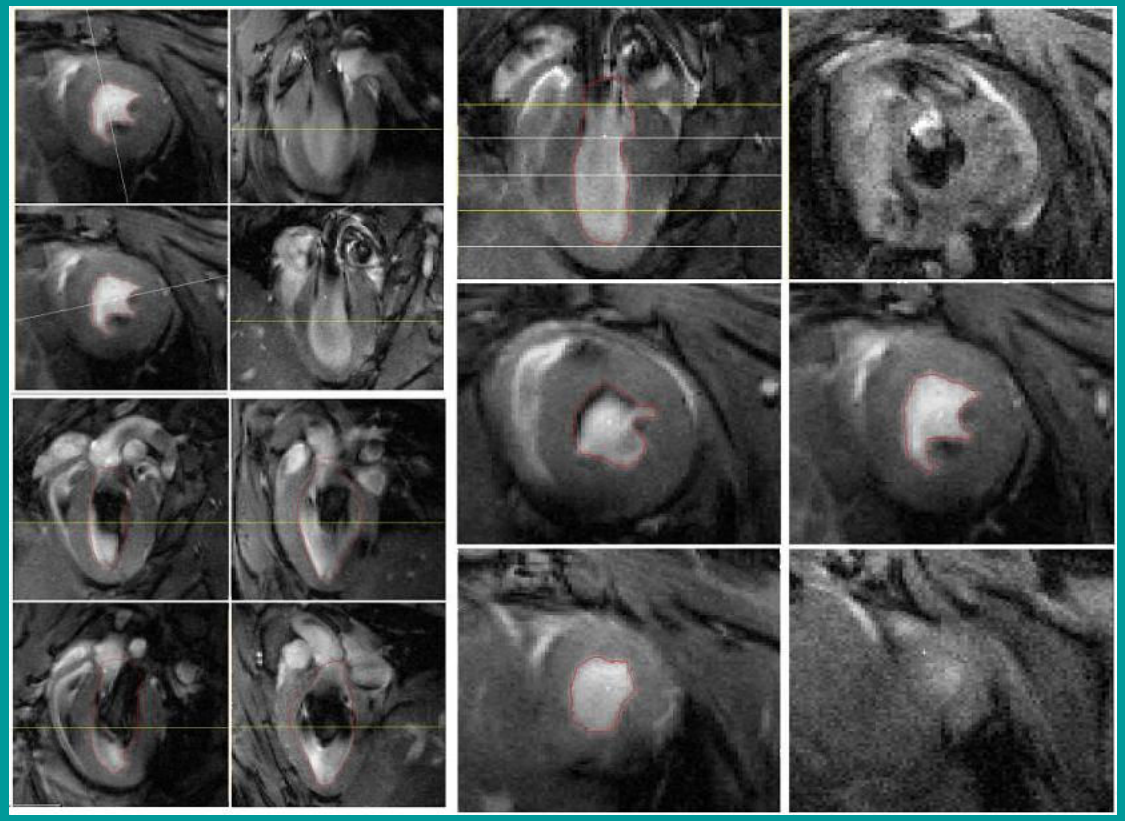


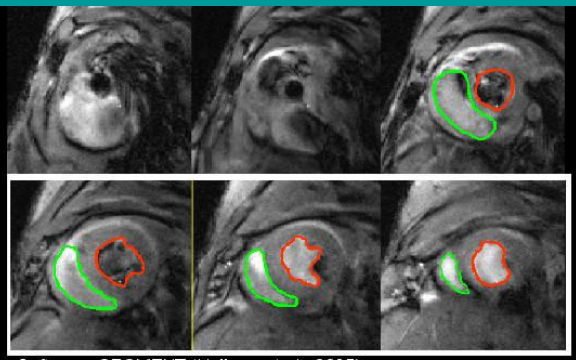
Part of right ventricle missing



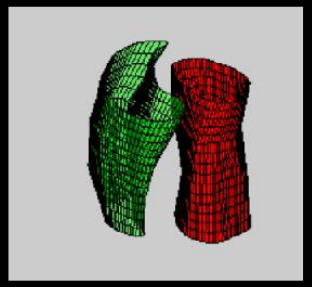


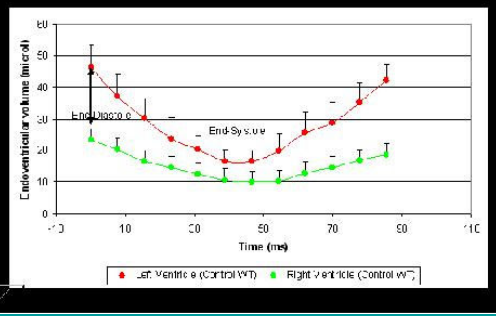
Short-axis acquisitions – underestimate right ventricular volume…our analysis is based on three mid-axis views





Software: SEGMENT (Heiberg et al., 2005)





Data based on 6 control male WT mice & prospective MRI acquisitions..

And at the end of all that

- Observe well . . .
- and carefully, what the *instruments* can reveal,
- all we know is what we see.
- There is no other truth.

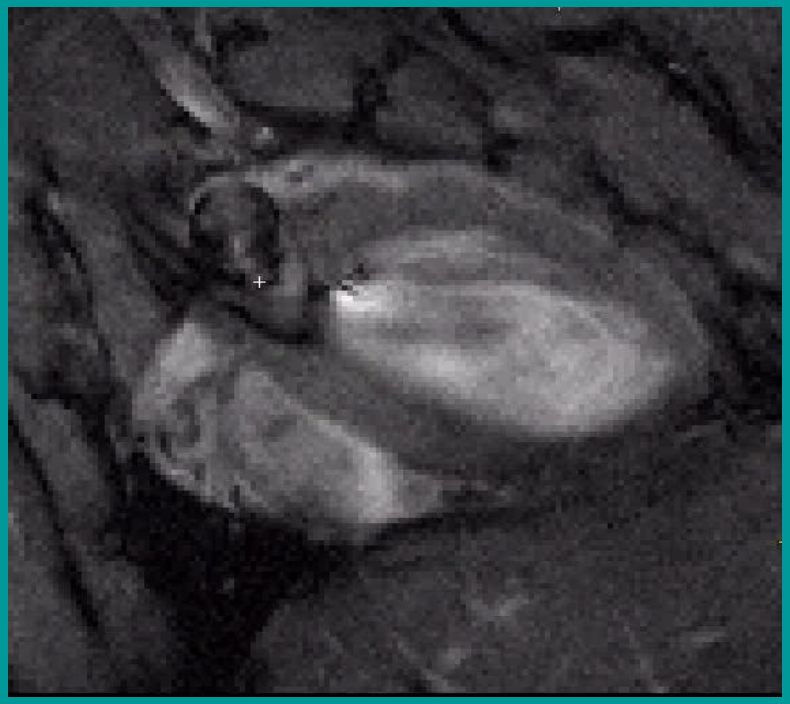
Support

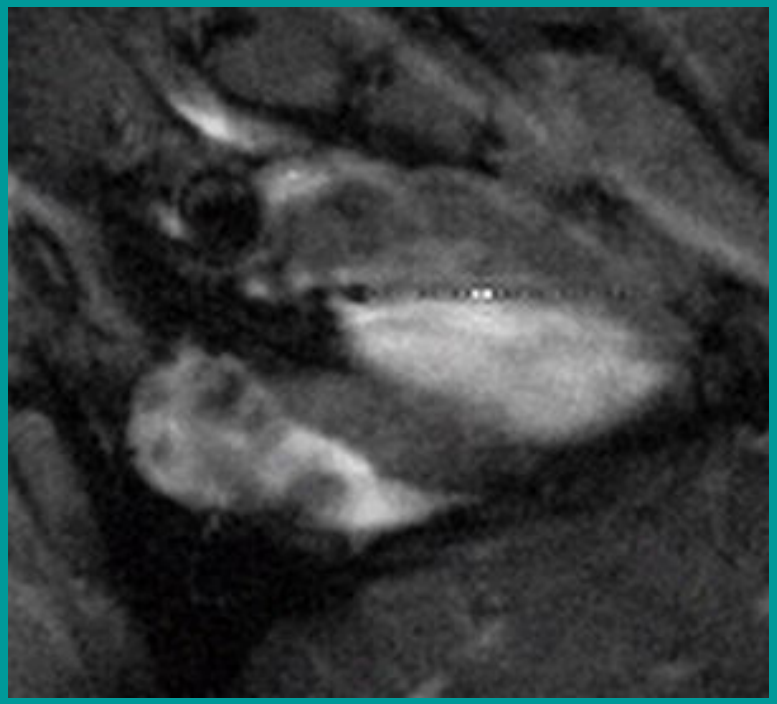
- Department of Energy Office of Science and Biological Research (Contract No. DE-AC02-98CHI-886
- New York State Office of Science, Technology and Academic Research

New positioning system

Designed by Dr. S. D. Smith and produced in collaboration with T. Lambertson @ Central Shops, BNL

MRI *can* image moving subjects



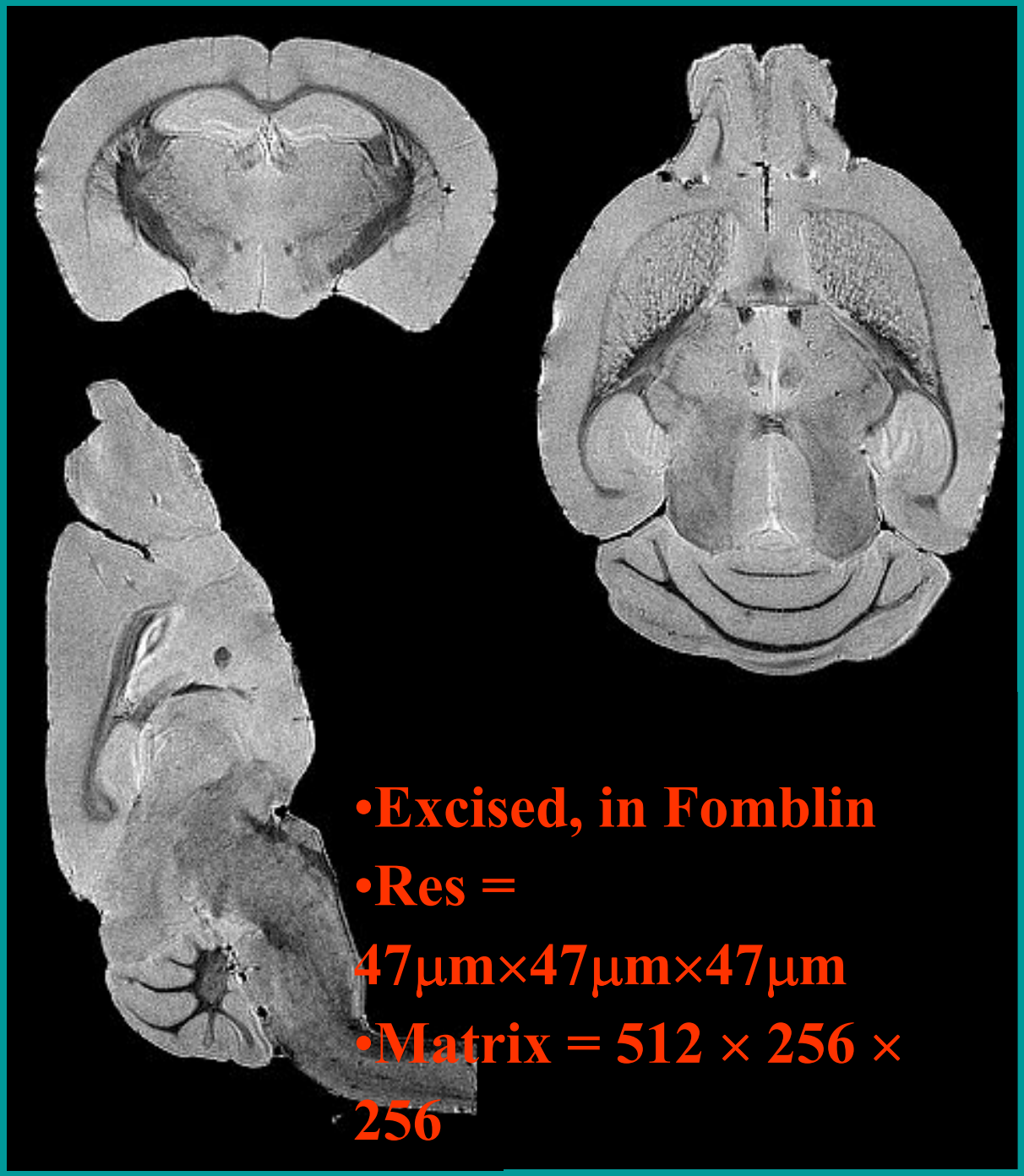


MR Microscopy & Informatics

In collaboration with:

Dr. Yu Ma (SBU, BNL)
BNL ITD (Drs. Bennett, McGuigan, Slatest)
Dr. Stephen J. Blackband (UFL)
Dr. P. Hof (MSSM)

In Vitro Magnetic Resonance Microscopy



- Bruker (UFL): 17.6 T
- T2* Gradient Echo:

  TE=7.5ms;

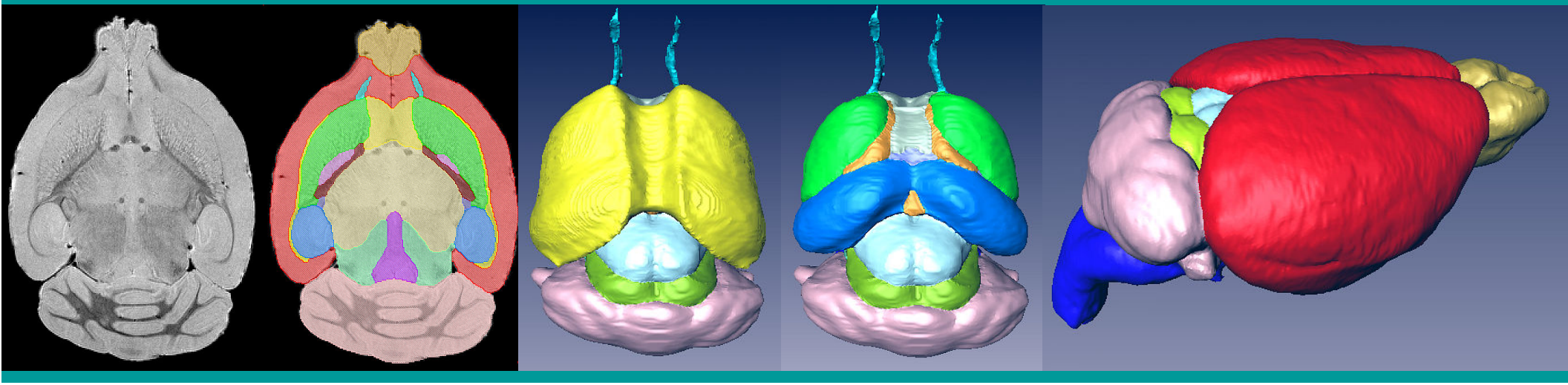
  TR=150ms;

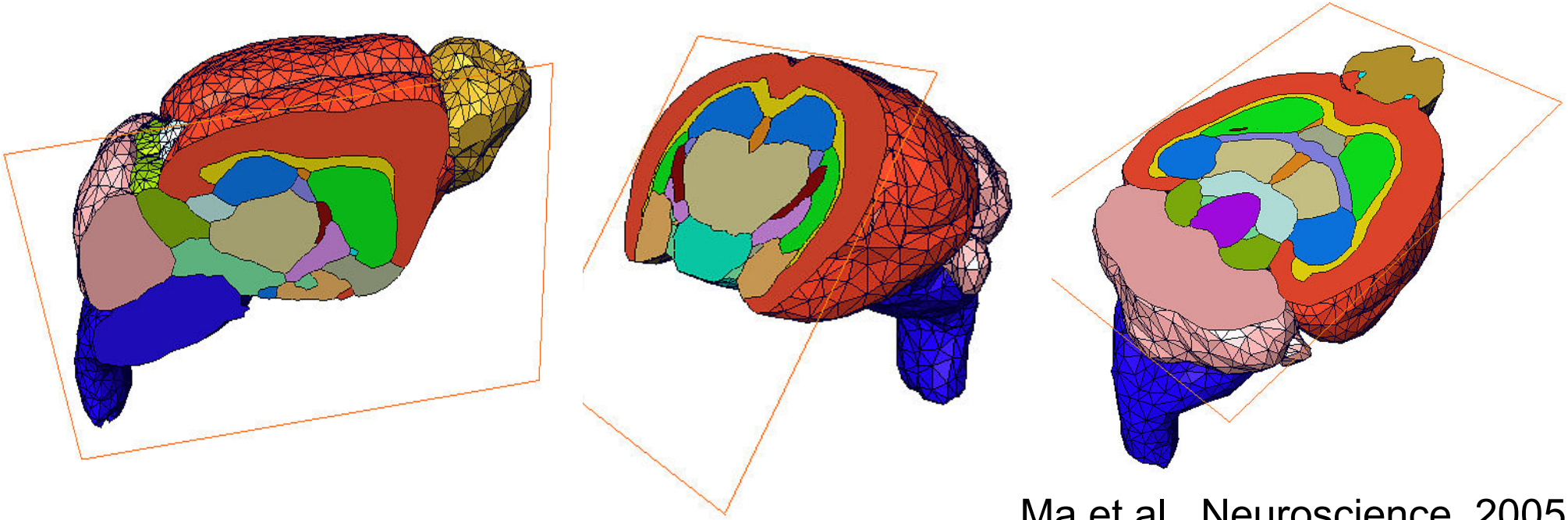
  FOV = 2.4x1.2x1.2cm;

  NEX = 2;

  AQT = 5.5hrs.

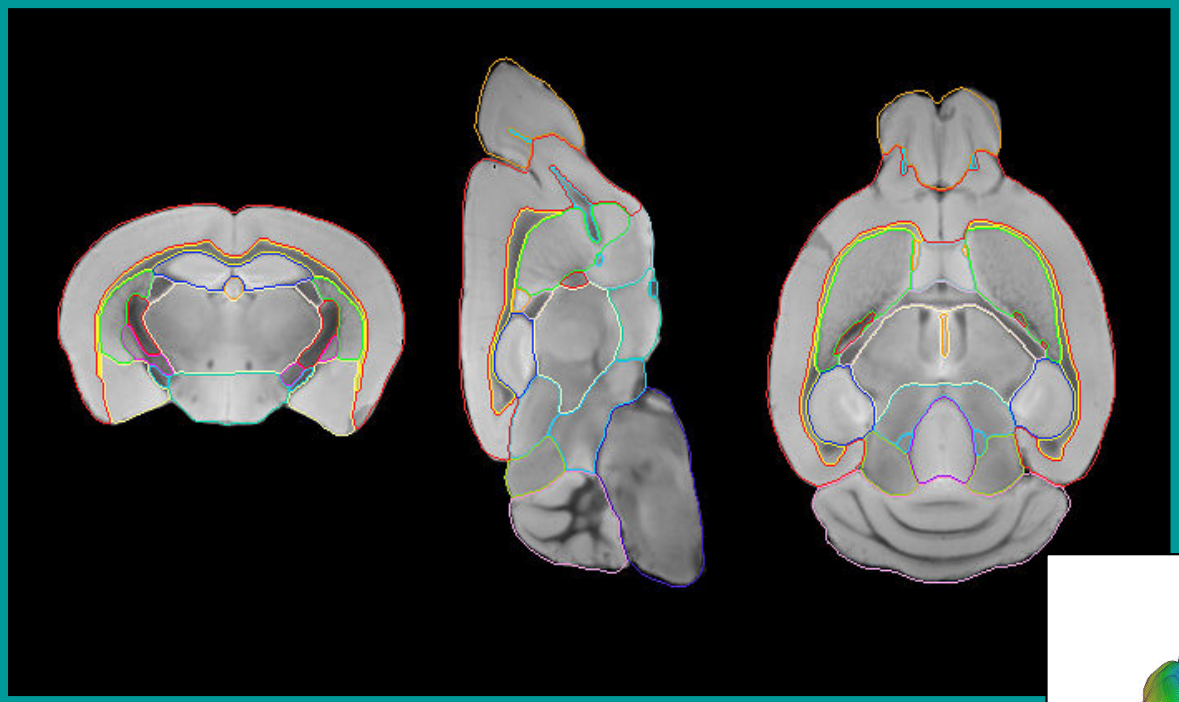
3D Normal Mouse Brain Atlas

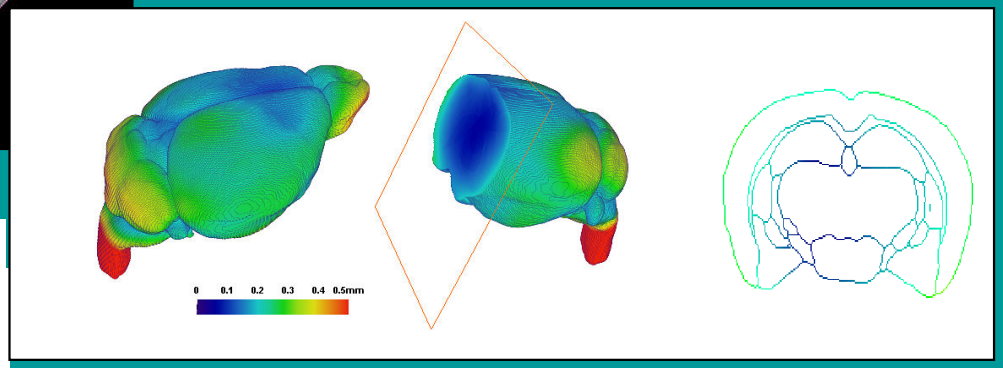


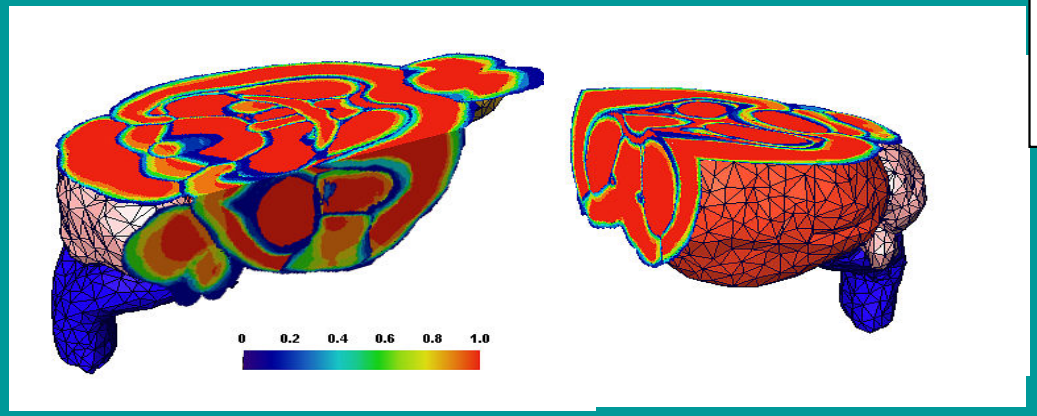


Ma et al., Neuroscience, 2005

Average Atlas and Probabilistic Atlas (n = 10)







Ma et al., Neuroscience, 2005

Mouse atlas: www.bnl.gov/ctn/mouse

Adult C57BL/6J Mouse Brain 3-D Digital Atlas - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address http://dev.bnl.gov/ctn/mouse/

Center for Translational Neuroimaging

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- MRI Research
- Transcranial Magnetic Stimulation
- Neuropsychoimaging
- Optical Imaging
- Awake Animal Imaging
- GVG and Addiction
- Behavioral Pharmacology & Neuroimaging
- Obesity & Eating Disorders
- Recent Publications

People
- Scientific Staff
- Graduate Students / Post-doctorals

Research Facilities
- MicroMRI Laboratory
- MicroPET Laboratory
- Microdialysis Laboratory

Adult C57BL/6J

3D MRI Digital Atlas Database of Adult C57BL/6J Mouse Brain

To take advantage of the information emerging from the mouse genome sequencing efforts, it has become necessary to systematically collect normative phenotypic information at all biological levels. Accordingly, an international collaboration, the Mouse Phenome Database (MPD) project, was created to establish a collection of baseline phenotypic data from commonly used inbred mice, such as the C57BL/6J, 129S1/SvImJ, DBA/2J and BALB/cByJ strains. The National Institutes of Health (NIH) neuroimaging phenotyping informatics emphasis has similarly been directed toward designing comprehensive three dimensional (3D) digital brain atlases of commonly used mice strains including variability of brain structures across a given strain.

As part of this world-wide effort, we have constructed an adult male C57BL/6J mouse brain atlas database derived directly from T2*-weighted 3D magnetic resonance microscopy images acquired on a 17.6-T magnet @ University of Florida. The 3D neuroanatomical information of twenty segmented structures including structure variability data, are integrated into a comprehensive database with the following framework:

- Multiple brain samples with T2*-weighted 3D magnetic resonance microscopy images.

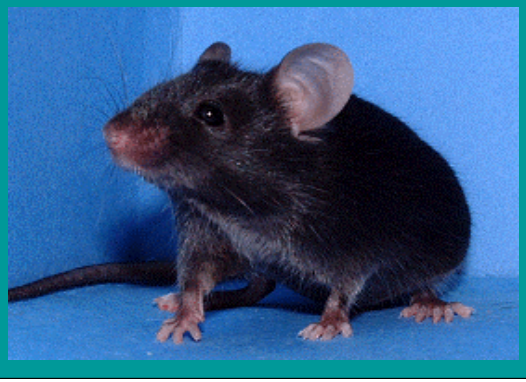
Atlas Database Links
- Procedure of Atlas Creation
- Mouse Brain Atlas Database
- Visualization Tool
- Authors and Collaborators
- MR microscopy @ AMRIS, University of Florida

Local intranet

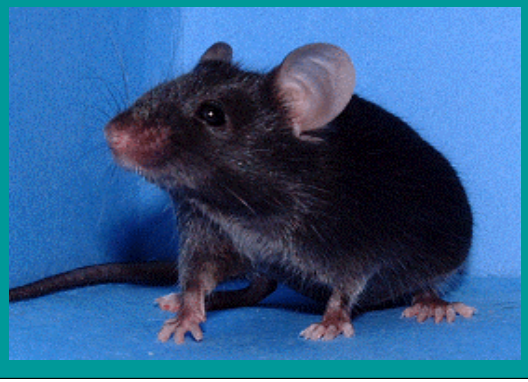
Ma et al., Neuroscience 2005

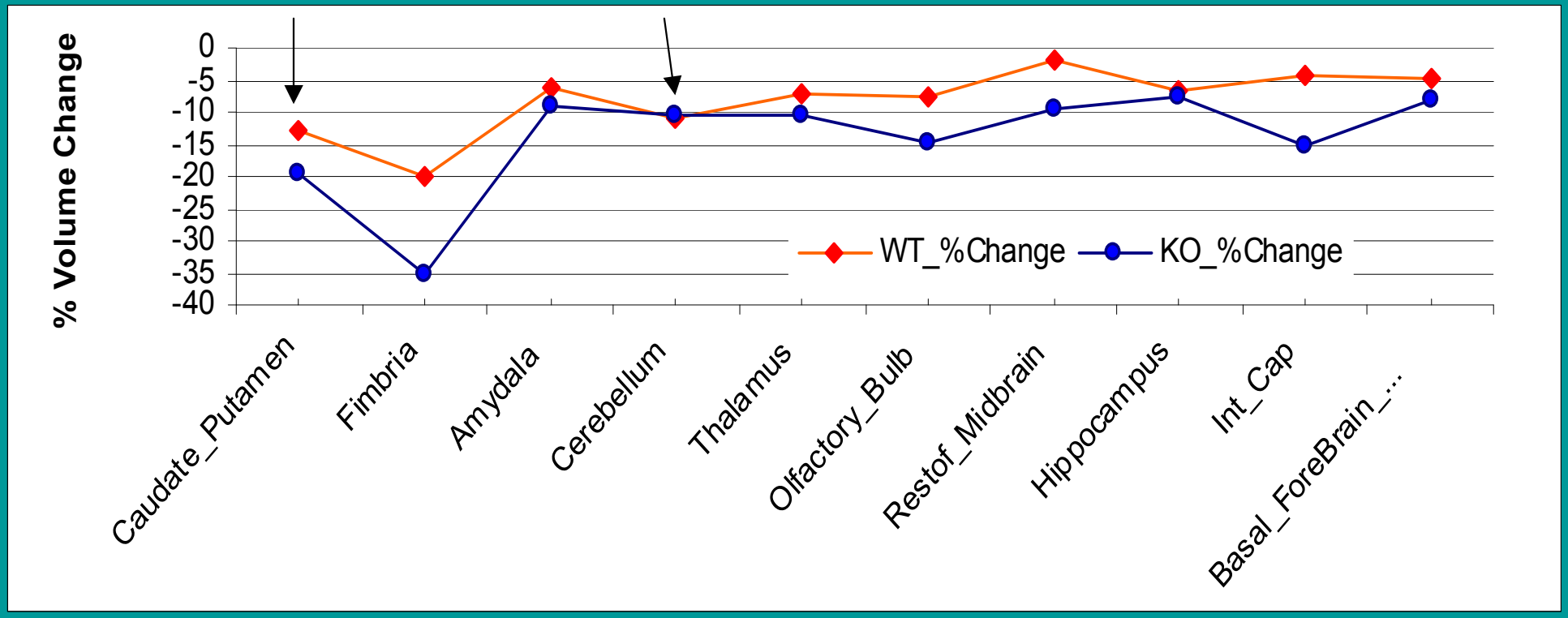
ADHD mouse model: neonatal 6-OHDA lesion

WT + 6-OHDA lesion
(hyperactive)

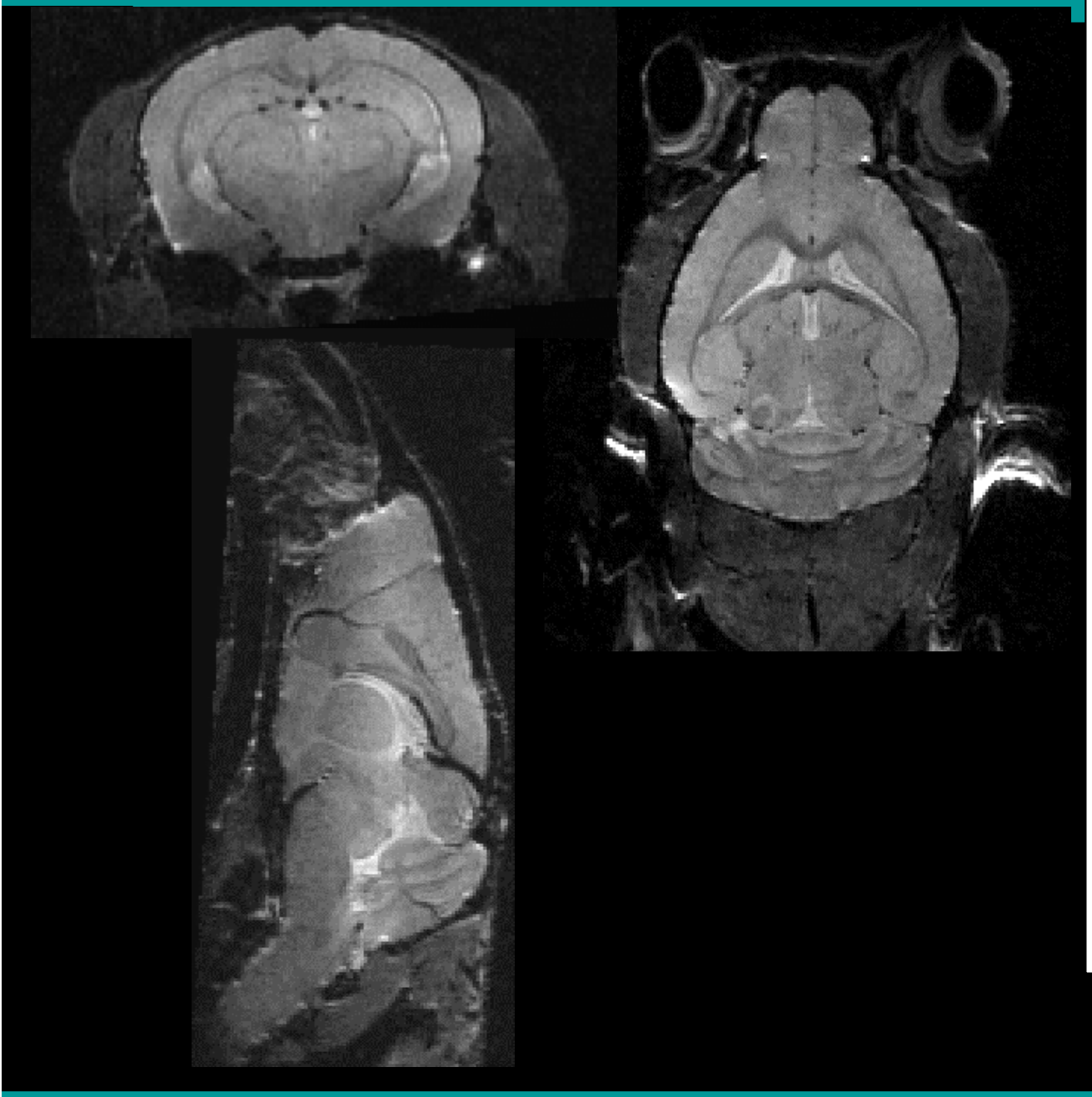


Dopamine 4 deficient + 6-OHDA lesion
(not hyperactive)





In Vivo Magnetic Resonance Microscopy



- Bruker: 9.4 T
- Spin_Echo(MSME)
- TE=30ms;
- TR=400ms;
- FOV =2.8×2.4×1.35cm^3;
- Matrix = 256×256×128
- Resolution ~ 109x94x105μm^3
- NEX = 1;
- AQT = 3hrs.
- Fat Suppression=On
- Flip Angle=145°

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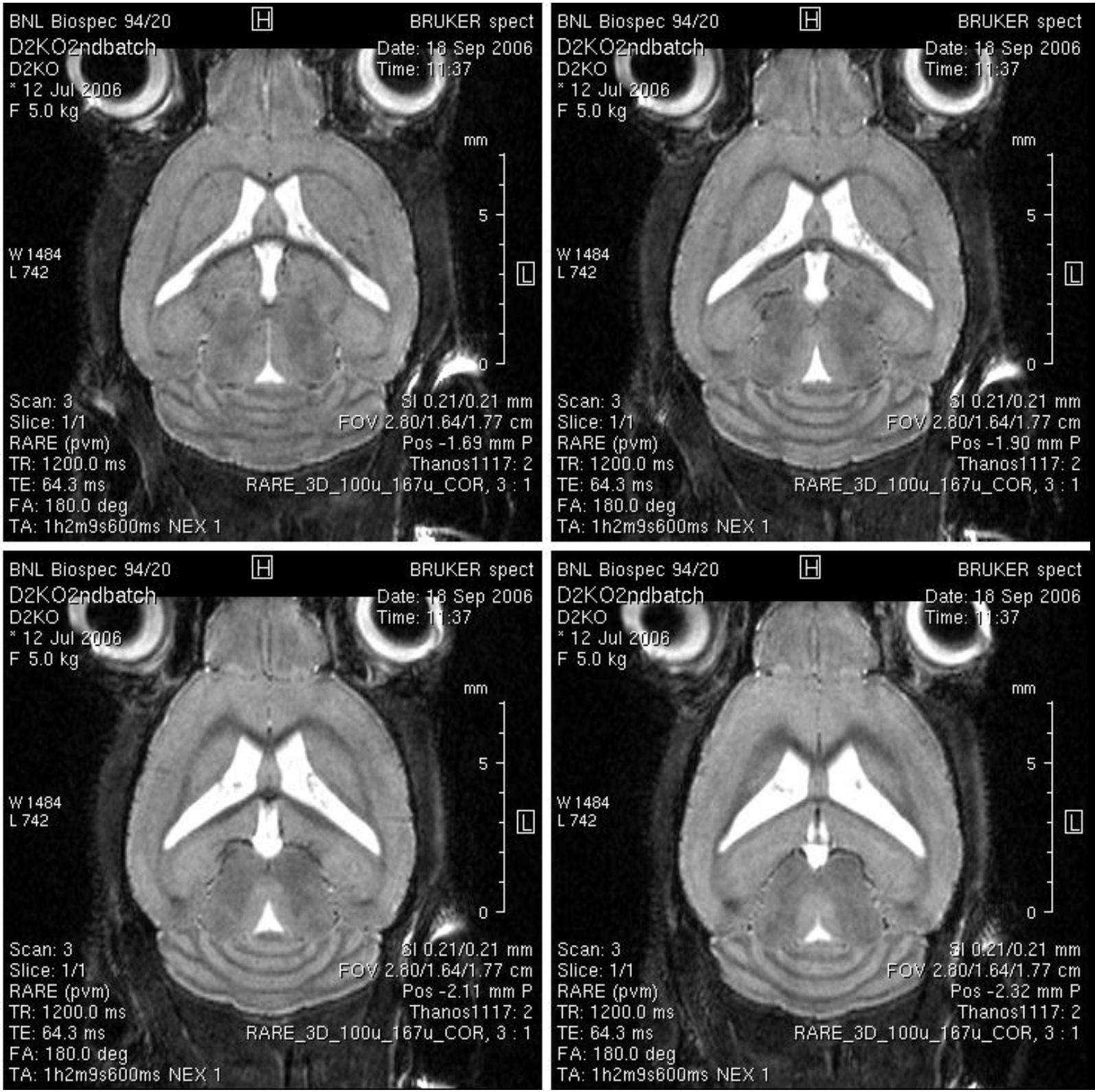
BNL Biospec 94/20
H
BRUKER spect
D2KO2ndbatch
Date: 18 Sep 2006
D2KO
Time: 11:37
* 12 Jul 2006
F 5.0 kg
mm
5
0
W 1484
L 742
L
Scan: 3
SI 0.21/0.21 mm
Slice: 1/1
FOV 2.80/1.64/1.77 cm
RARE (pvm)
Pos -1.69 mm P
TR: 1200.0 ms
Thanos1117: 2
TE: 64.3 ms
RARE_3D_100u_167u_COR, 3 : 1
FA: 180.0 deg
TA: 1h2m9s600ms NEX 1
BNL Biospec 94/20
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BRUKER spect
D2KO2ndbatch
Date: 18 Sep 2006
D2KO
Time: 11:37
* 12 Jul 2006
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W 1484
L 742
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Scan: 3
SI 0.21/0.21 mm
Slice: 1/1
FOV 2.80/1.64/1.77 cm
RARE (pvm)
Pos -1.90 mm P
TR: 1200.0 ms
Thanos1117: 2
TE: 64.3 ms
RARE_3D_100u_167u_COR, 3 : 1
FA: 180.0 deg
TA: 1h2m9s600ms NEX 1
BNL Biospec 94/20
H
BRUKER spect
D2KO2ndbatch
Date: 18 Sep 2006
D2KO
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Scan: 3
SI 0.21/0.21 mm
Slice: 1/1
FOV 2.80/1.64/1.77 cm
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TA: 1h2m9s600ms NEX 1
BNL Biospec 94/20
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D2KO2ndbatch
Date: 18 Sep 2006
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Time: 11:37
* 12 Jul 2006
F 5.0 kg
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L 742
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Scan: 3
SI 0.21/0.21 mm
Slice: 1/1
FOV 2.80/1.64/1.77 cm
RARE (pvm)
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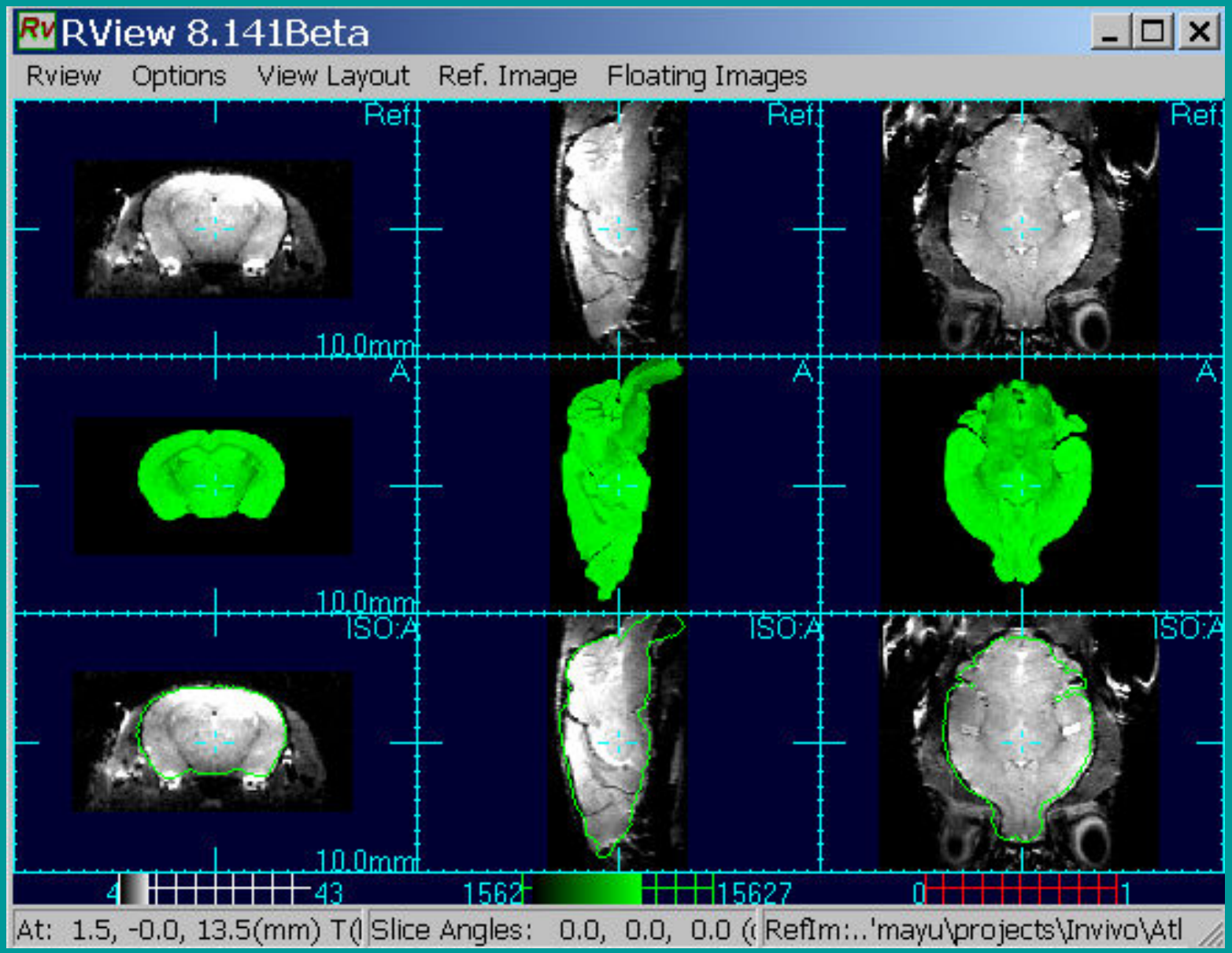
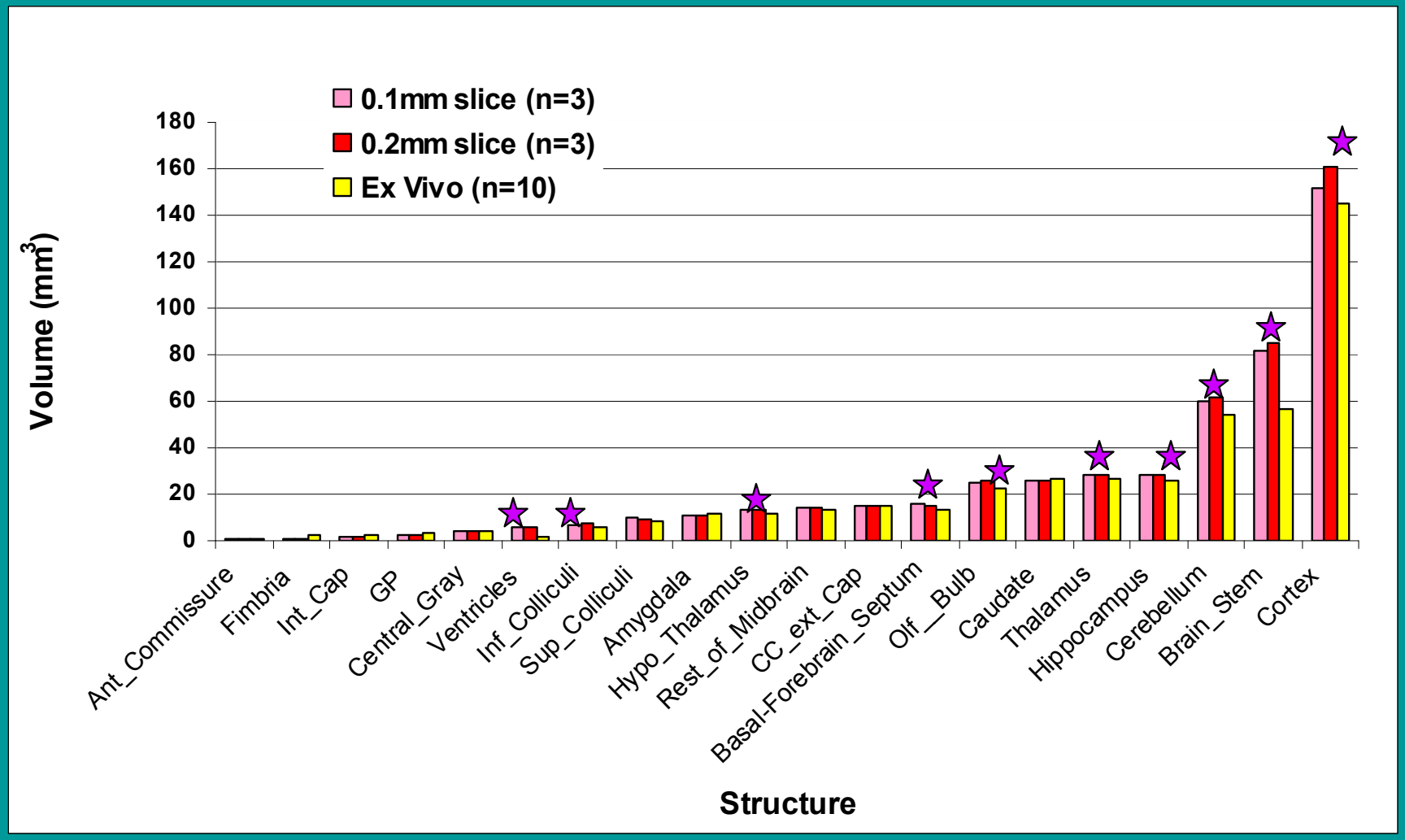
TR: 1200.0 ms
Thanos1117: 2
TE: 64.3 ms
RARE_3D_100u_167u_COR, 3 : 1
FA: 180.0 deg
TA: 1h2m9s600ms NEX 1

Creating the Atlas: From In Vitro to In vivo



Preliminary Results: Volume



Ex vivo: 10% decease in total brain volume; 74% decease in ventricle volume.

Vasoactive Intestinal Peptide – deficient mouse

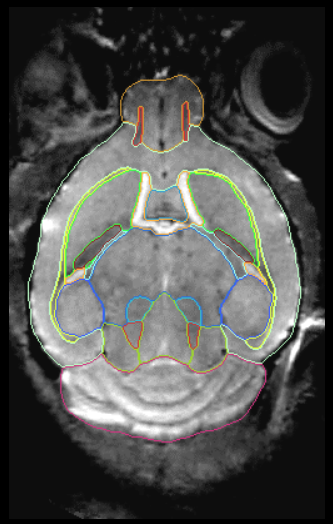
No optical tracks

Enlarged ventricles

VIP deficient mice phenotyping:

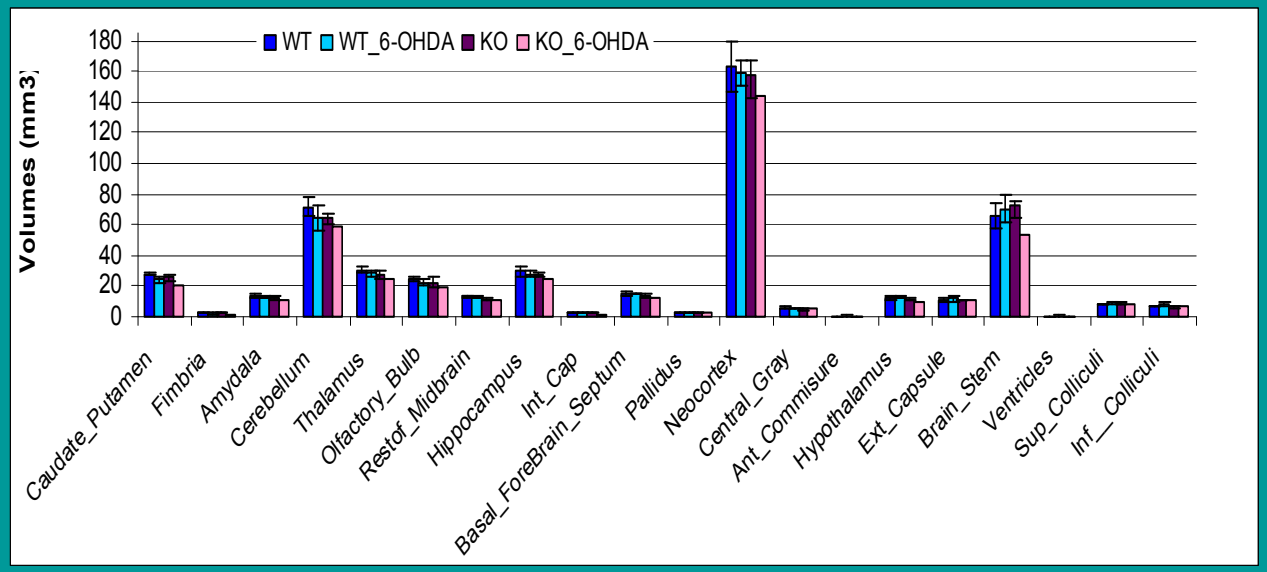
Primary pulmonary HTN

brain?



Szema, Benveniste, Said

ADHD



% Volume Change

Structure	% vol change (WT)	Effect size	% vol change (KO)	Effect size
Fimbria	-20.2%	-2.0	-35.1%	-3.7
Caudate Putamen	-12.7%	-3.6	-19.6%	-3.5
Cerebellum	-10.8%	-1.5	-10.3%	-2.3
Hippocampus	-6.5%	-1.0	-7.4%	-1.5

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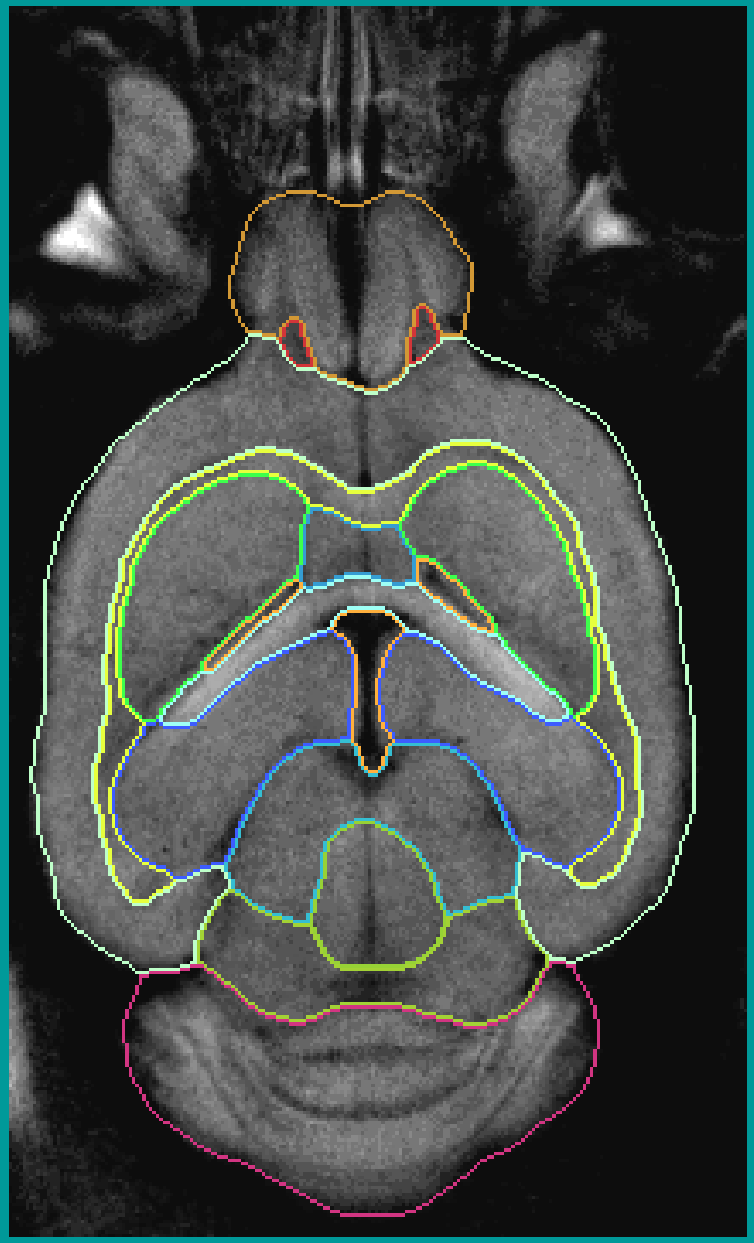
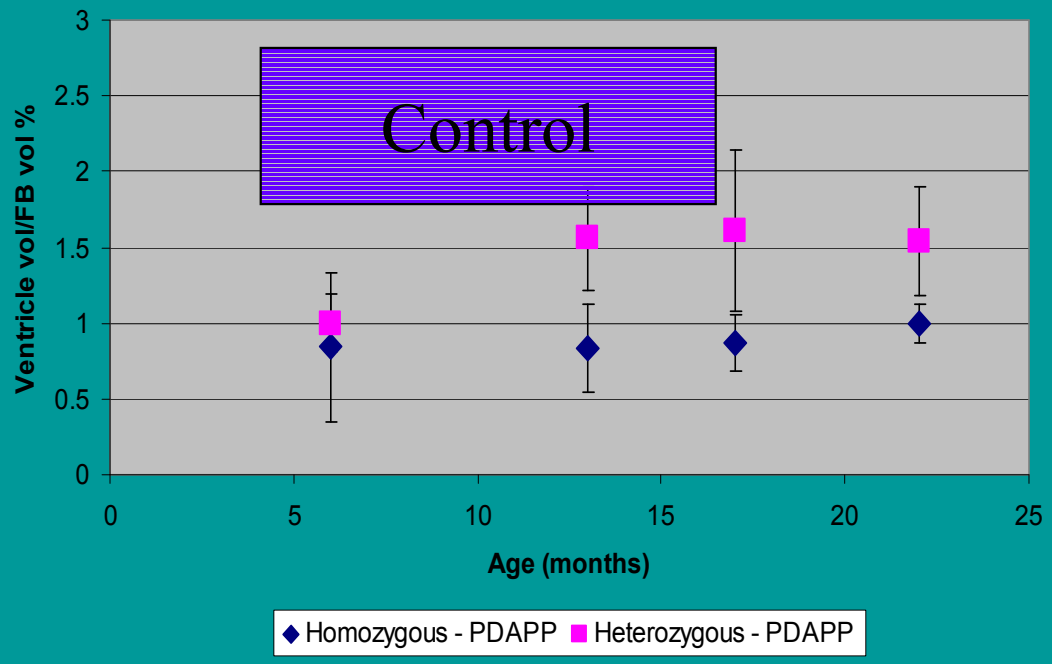
PDAPP mice:



Preliminary in vivo data:

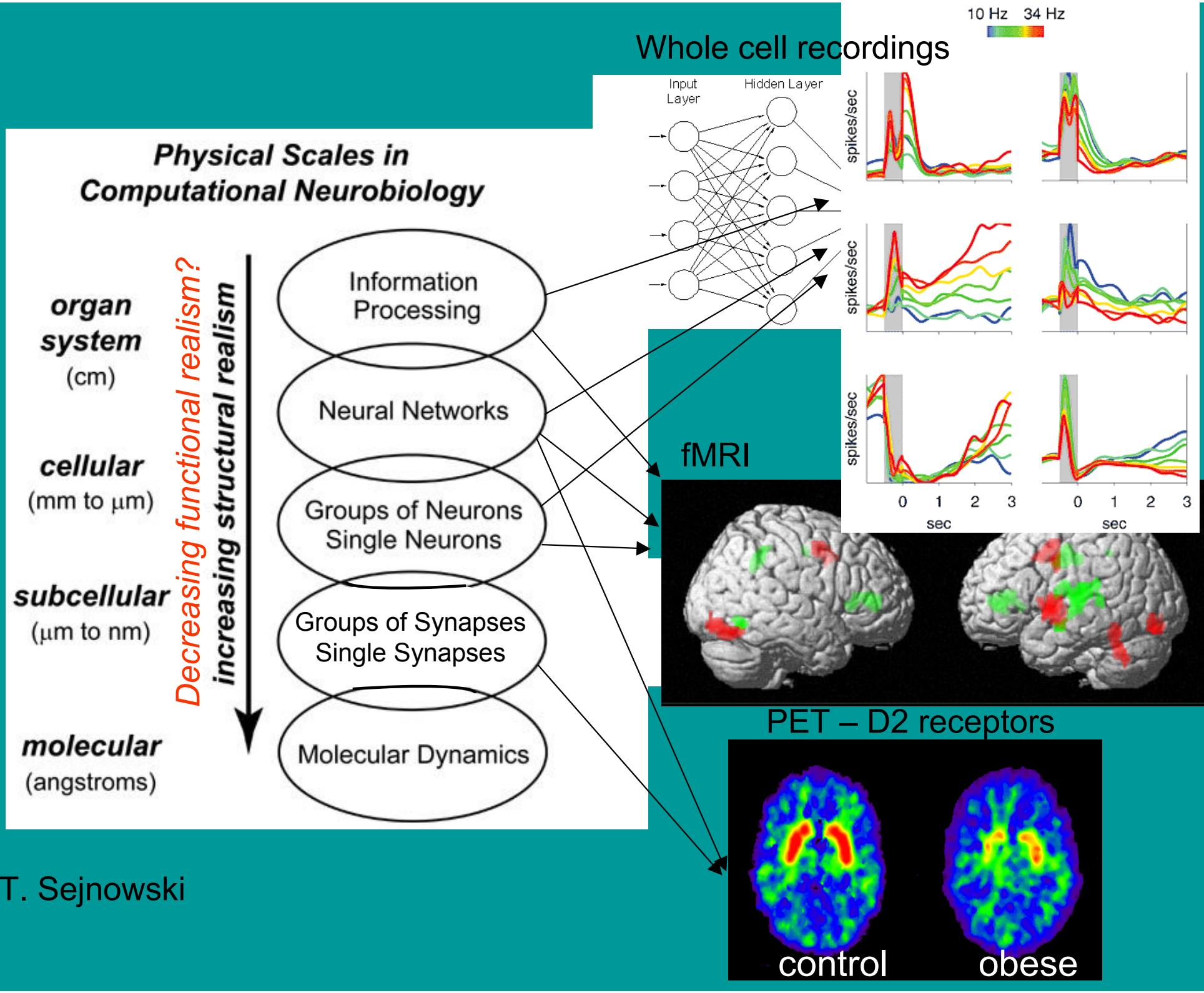
Ventricles smaller; no hippocampal atrophy even at 22 months of age.



Functional Brain Activation Studies

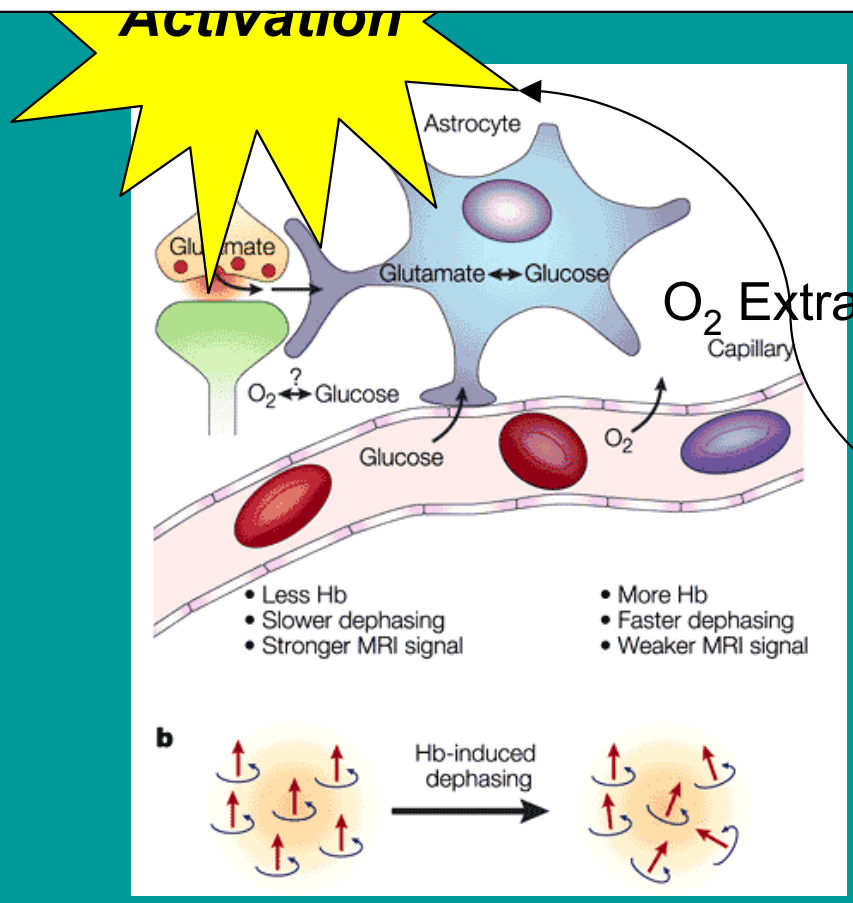
..combining fMRI and optics..
….correlating $[Ca^{++}]_i$ transients with the BOLD signal…

Benveniste, Smith & Du


Physical Scales in Computational Neurobiology
organ system (cm)
cellular (mm to μm)
subcellular (μm to nm)
molecular (angstroms)
Decreasing functional realism?
increasing structural realism
Information Processing
Neural Networks
Groups of Neurons Single Neurons
Groups of Synapses Single Synapses
Molecular Dynamics
Input Layer
Hidden Layer
Whole cell recordings
10 Hz
34 Hz
spikes/sec
sec
fMRI
PET – D2 receptors
control
obese

T. Sejnowski

Blood-Oxygen-Level-Dependent



O_2 Extraction, ***E***

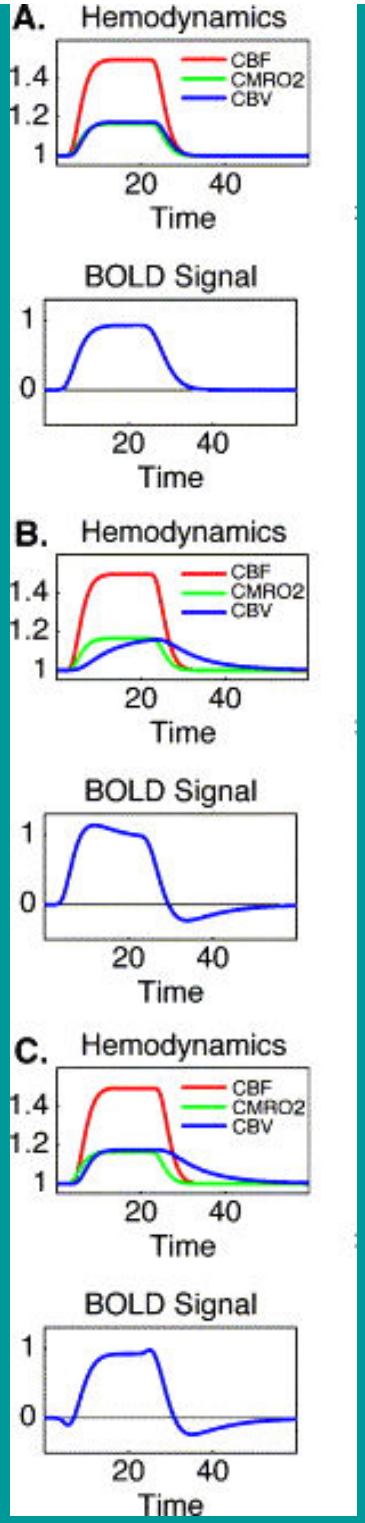
Following increased neuronal activity in the brain, the local cerebral blood flow (CBF) increases much more than the cerebral metabolic rate of oxygen ($CMRO_2$), and as a result ***E*** decreases with activation (Fox and Raichle, 1986).

Because the local blood is more oxygenated, there is less deoxyhemoglobin present, and the magnetic distortions are reduced, the local MR signal increases slightly….

Hgb-Oxy: diamagnetic

HgbR: paramagnetic - Creates magnetic field distortions within and around blood vessels

What is the BOLD signal representing?

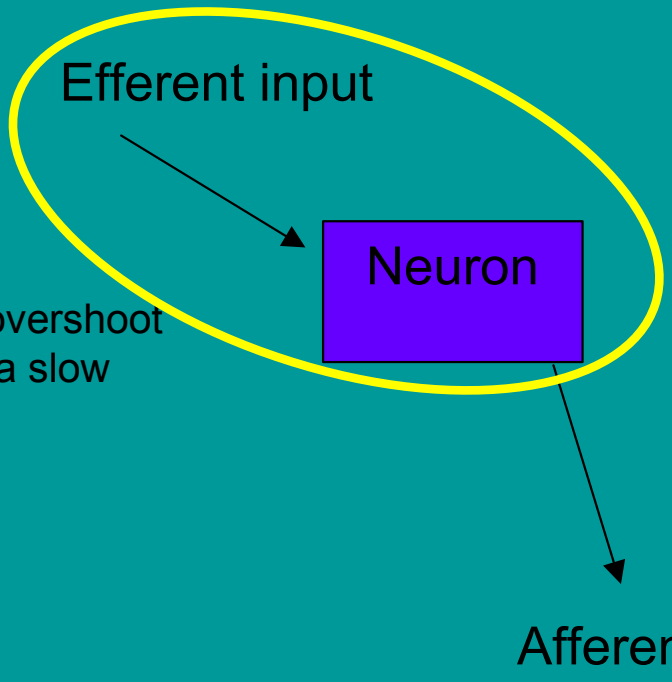


(A) a simple BOLD response in which the physiological changes have similar time courses;

(B) a BOLD response with an initial overshoot and poststimulus undershoot due to a slow CBV response

(C) a BOLD response with an initial dip as well, created by adding a 1-s delay of the CBF impulse response relative to the CMRO2 impulse response.

Buxton et al., 2004



Logothetis et al., 2004

..by the way..a Google search of “understanding the fMRI bold signal” yields 152,000 results….