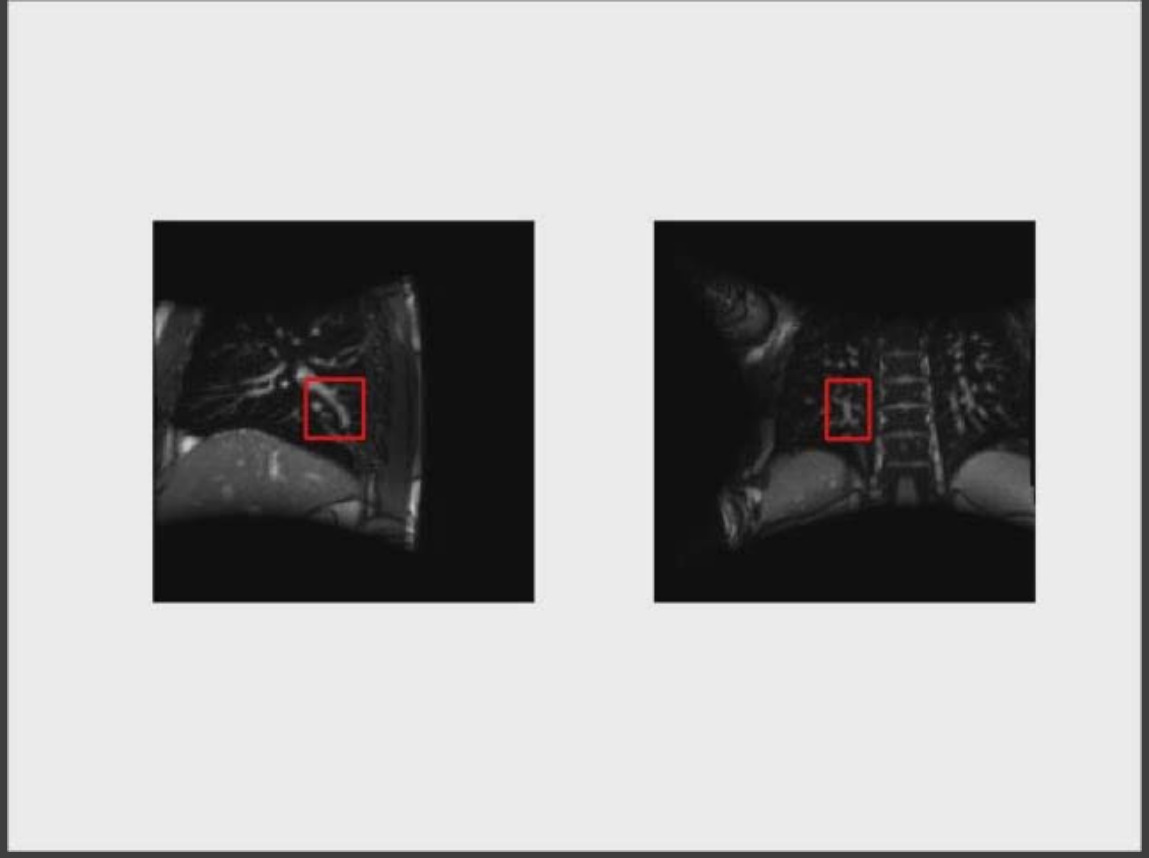

4D-MRI for Motion Management in Radiotherapy

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Outline

I: Introduction: 4D-CT deficiencies; motivations for/pitfalls of “4D-MRI”

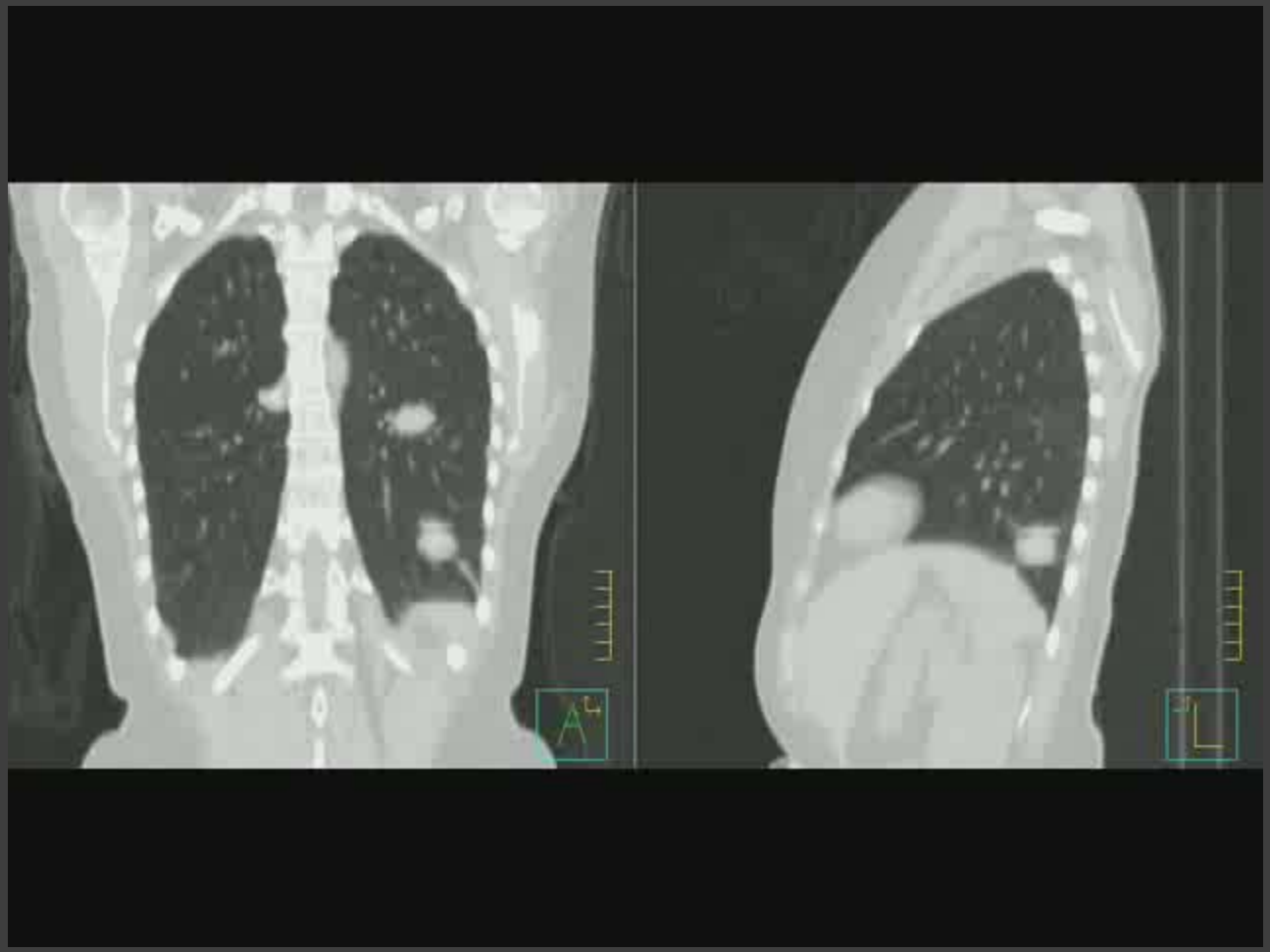
II: Selection of prior 2D dynamic MRI (dMRI) in radiotherapy

III: Selection of prior 2D-4D dMRI in radiotherapy

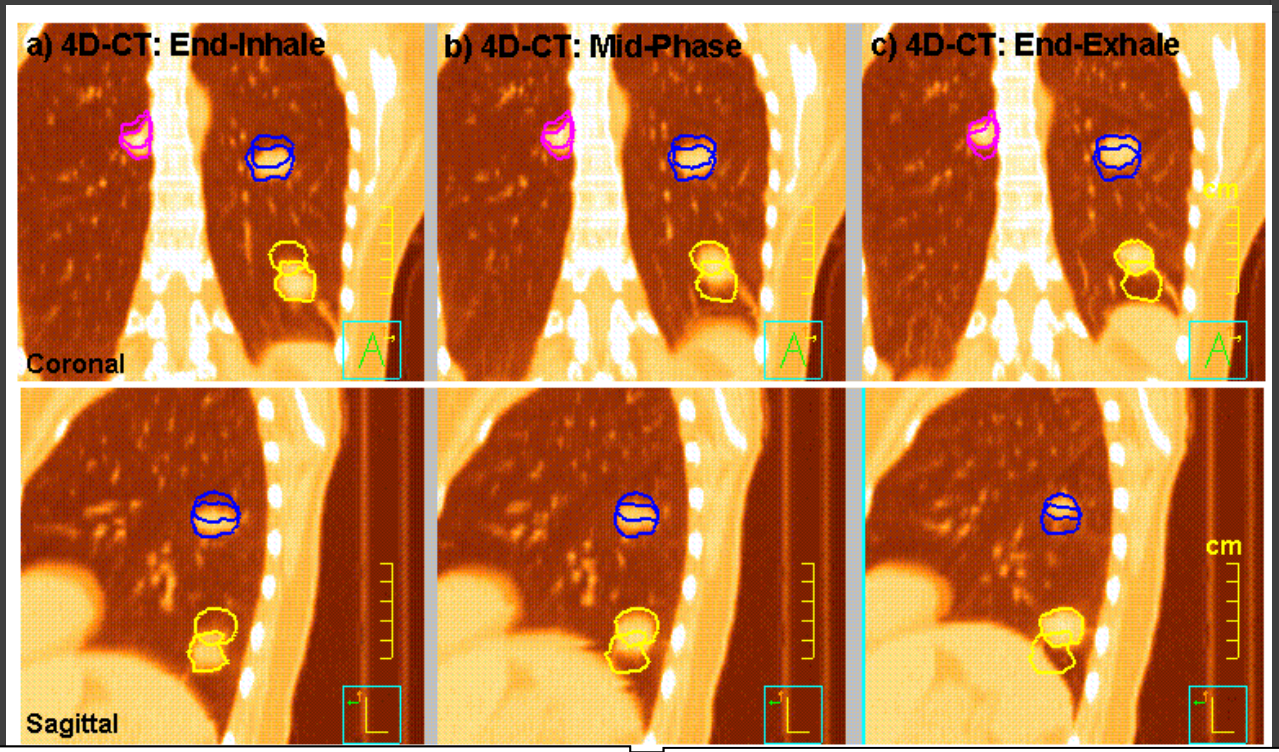
IV: “4D-MRI” methods development at John Hopkins

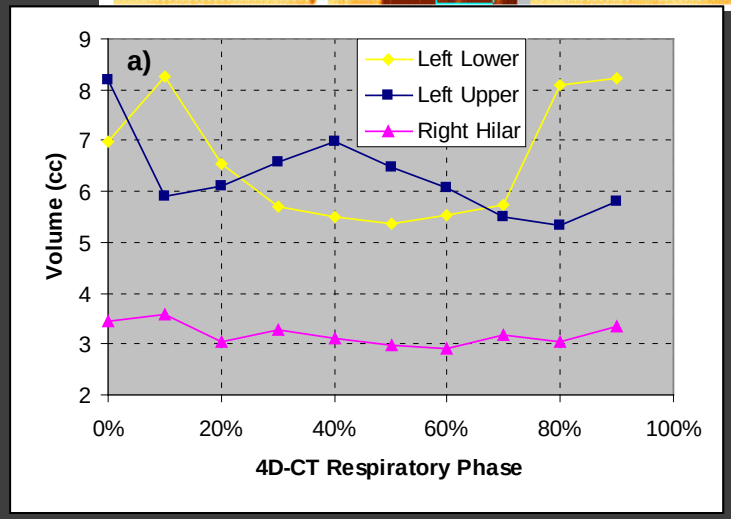
V: Concluding remarks

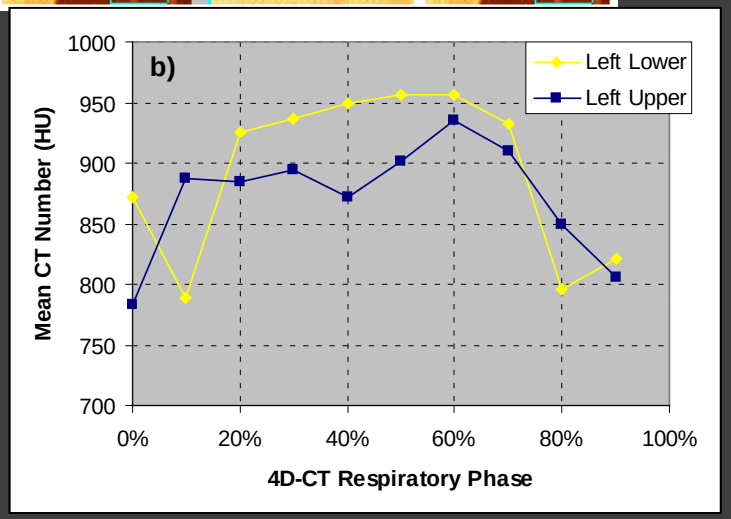
Introduction: Deficiencies of 4D-CT



I Introduction: Deficiencies of 4D-CT, cont'd.







Introduction: Motivations for "4D-MRI"

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- Non-ionizing, fast

- Allows for more complete motion characterization; likely can overcome pitfalls of 4D-CT, which represents a snap-shot in time and fails to address motion variability inherent to normal respiration

- Provides unique opportunities for validation studies of different management techniques (gating, breath-holding, tracking…)

- Offers possibilities for 4D tumor tracking as well as providing "representative" 4D anatomical imaging, as in 4D-CT

- Therefore, may be well suited for "4D" radiotherapy planning and further development

- Promises for MRI-guided RT: non-invasive real-time MR imaging of target will likely result in higher targeting accuracy and hence further margin reduction

Introduction: Pitfalls of "4D-MRI"

- Not widely available
- Cost-prohibitive?
- Geometric image distortions?
- Spatial resolution is more limited than CT (SNR tradeoffs)
- "4D-MRI" simulations likely take longer than present CT-based simulations
- Patient (dis-) comfort: body coils required are somewhat constrictive. MRI bores can cause claustrophobia (larger bore systems help)
- Not all patients can comply or are MRI-safe
- No standards for "4D-MRI"
- Therefore, no current support for "4D-MRI" in treatment planning systems

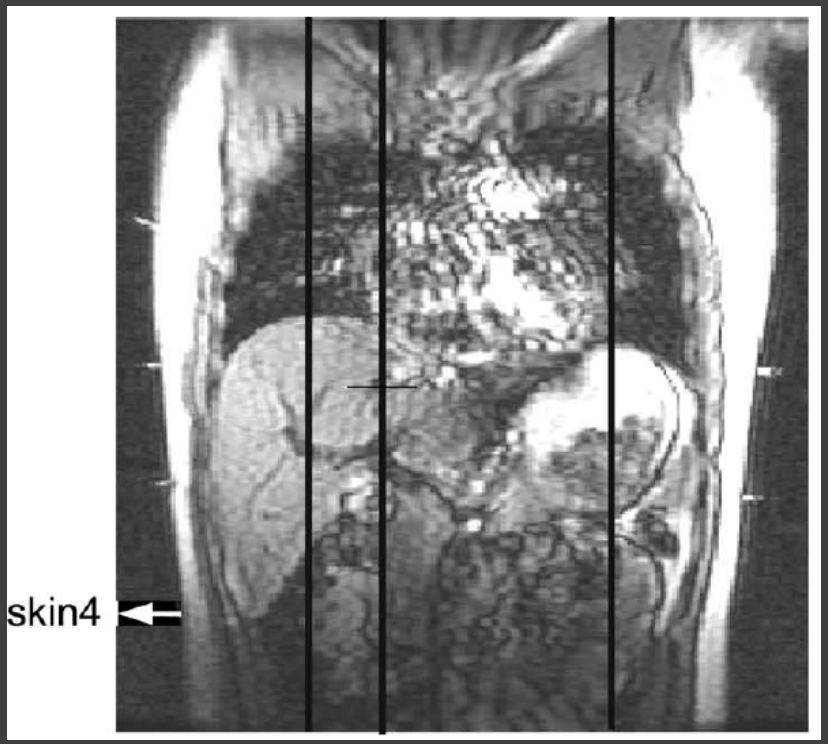
Early adopters must address these issues while demonstrating dosimetric/safety/clinical benefit

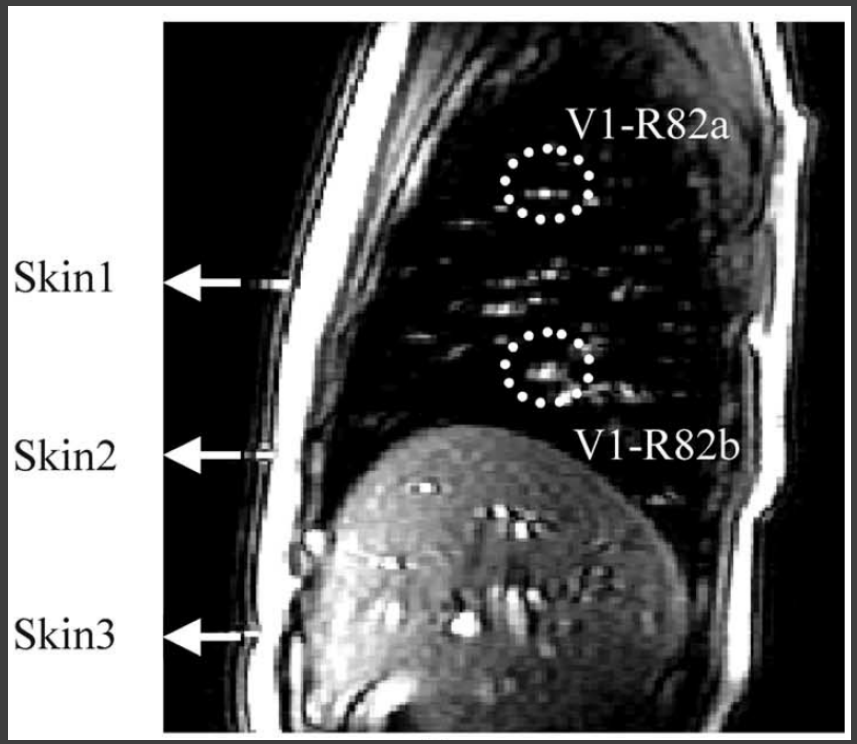
II. Review of selection of 2D dynamic MRI studies:

1. **Lung: Koch et al. [IJROBP 2004; 60 (5): 1459]**
2. Pancreas: Feng et al. [IJROBP 2009; 74 (3): 884]
3. Liver: Kirilova et al. [IJROBP 2008; 71 (4): 1189]
4. Lung: Cai et al. [PMB 2007; 52: 365]
   [IJROBP 2007; 60(3): 895]

2D dMRI review: Koch et al. IJROBP 2004; 60 (5): 1459

- Thoracic 2D dMRI study in 3 volunteers and 4 lung cancer patients
- Skin markers monitored simultaneously with lung vessels on sagittal frames
- Cross-correlation-based vessel tracking



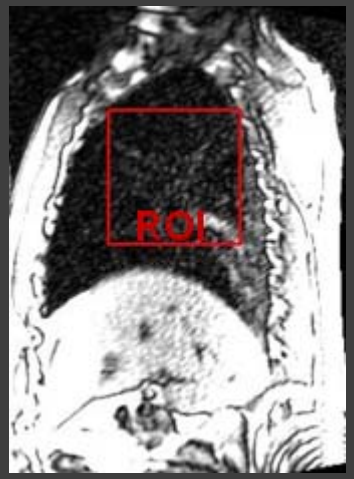


- 1.5 T (GE Signa)
- Fast gradient echo sequence
- TR: 4.0 ms; TE: 2 ms
- Flip angle: 60 degrees

- Pixel size: 1.6^2 mm^2
- Slab thickness: 10 mm
- Acq. speed: 450 ms/frame
- 100 frames per cine series

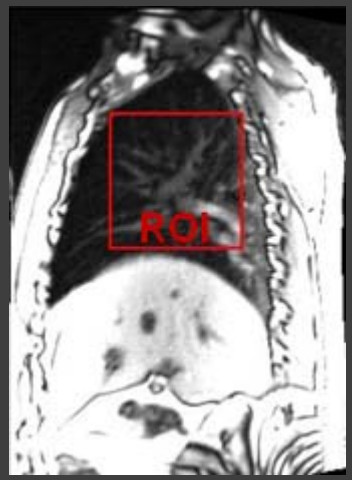
What is a "cross-correlation" in image processing?

Live image (k)



<pixel-wise (*i,j*) comparison>

Template image (N)

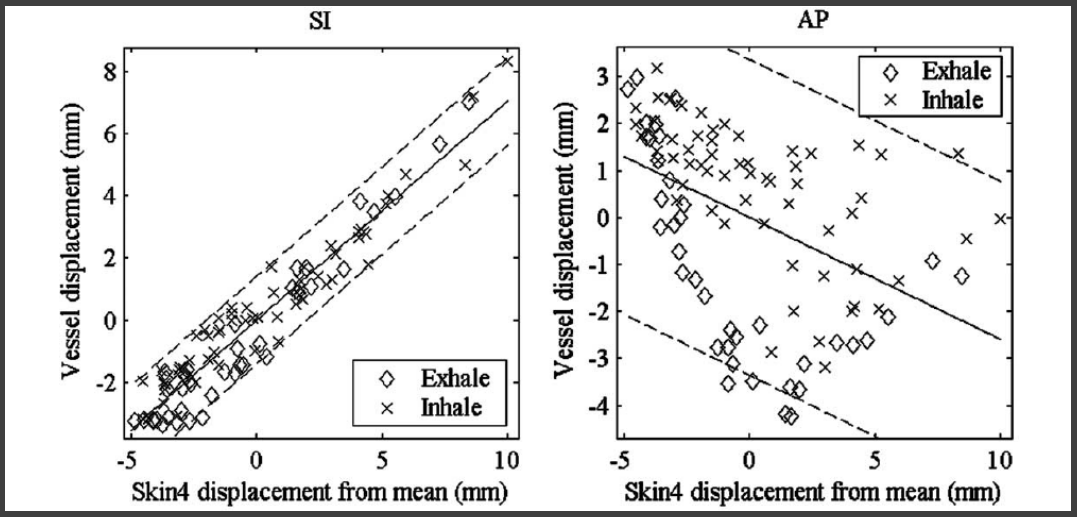


Normalized cross-correlation:

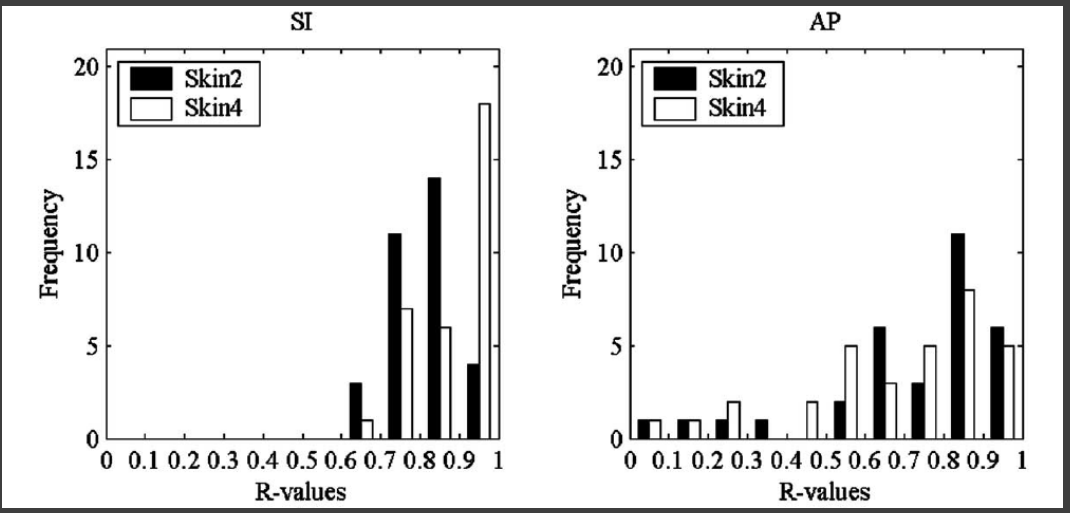
$$ncc_{k,N} = \sum_{i,j} (I_k \cdot I_N) \; / \; \sqrt{\{\sum_{i,j} (I_k \cdot I_k) \times \sum_{i,j} (I_N \cdot I_N)\}}$$

2D dMRI review: Koch et al. IJROBP 2004; 60 (5): 1459

One vessel vs. Skin4 marker for patient 3:



All vessels, all volunteers, vs. Skin2 and Skin4:



Conclusions:

- Best correlation observed between lung SI and mid-upper abdo skin
- Poorer lung-skin correlation in AP
- Significant inter-subject variability
- "Movement of an external fiducial may not correlate fully with, or predict, internal lung motion."

II. Review of selection of 2D dynamic MRI studies:

1. Lung: Koch et al. [IJROBP 2004; 60 (5): 1459]
2. **Pancreas: Feng et al. [IJROBP 2009; 74 (3): 884]**
3. Liver: Kirilova et al. [IJROBP 2008; 71 (4): 1189]
4. Lung: Cai et al. [PMB 2007; 52: 365]
   [IJROBP 2007; 60(3): 895]

2D dMRI review: Feng et al. IJROBP 2009; 74 (3): 884

- 2D dMRI Study in 17 unresectable pancreatic cancer patients
- Images obtained prior to and during chemo-radiation
- Simultaneous monitoring of diaphragm, abdominal wall and tumor borders to examine position correlations

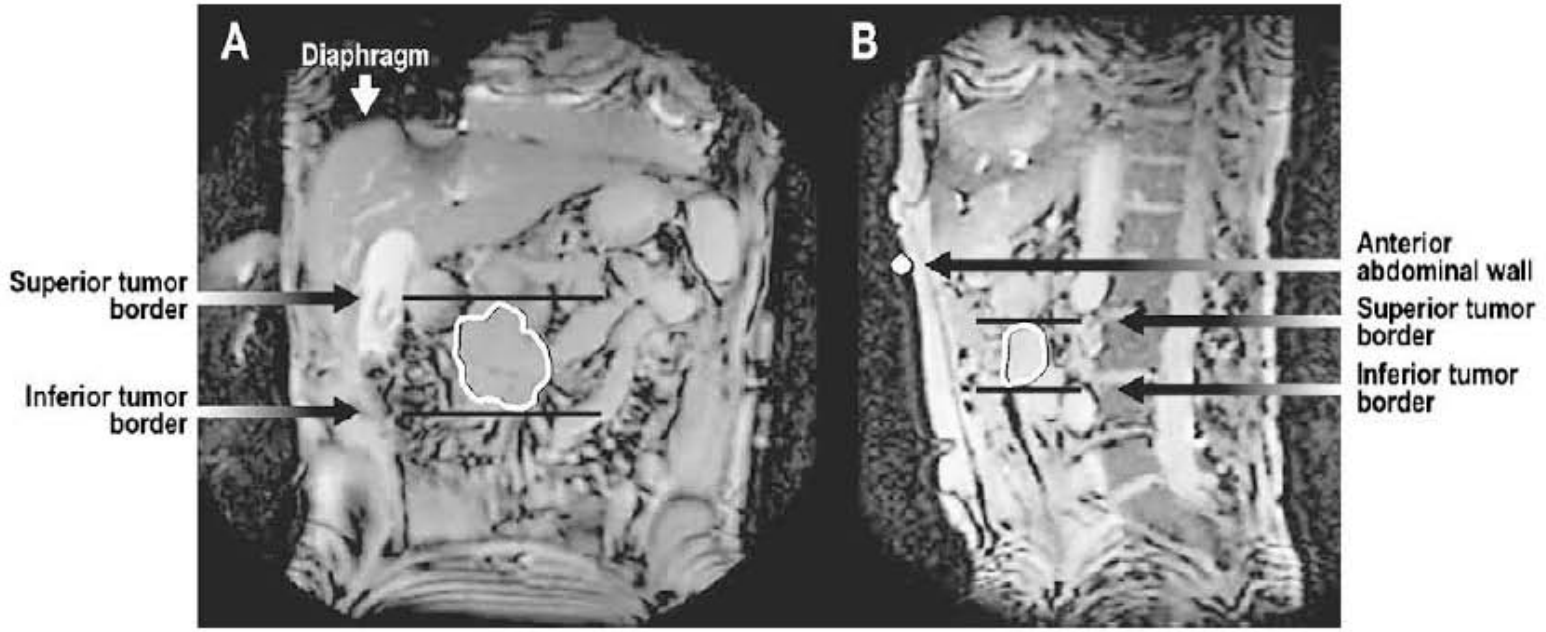
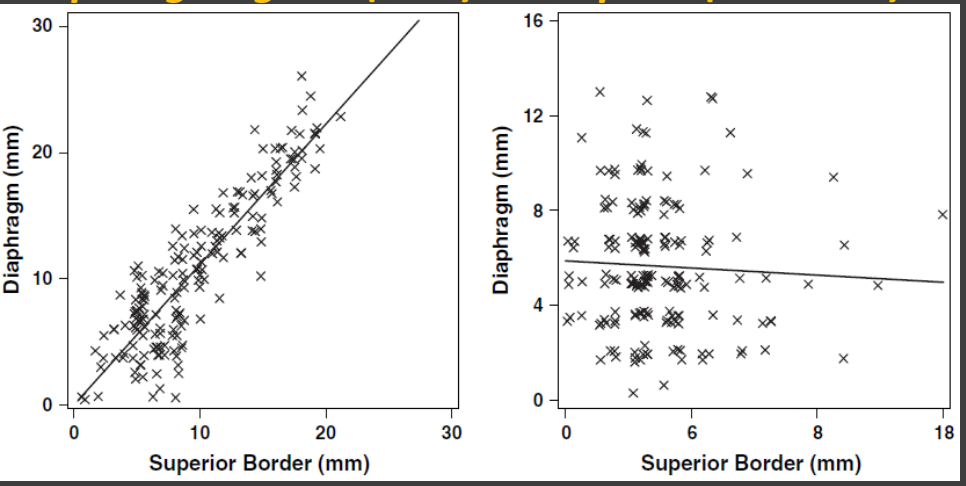


Fig. 1. (A) The tumor is contoured on a coronal image. The superior and inferior tumor borders are marked, as is the diaphragm. (B) In addition to the tumor contour and superior and inferior borders, the abdominal wall is marked.

- 3 T
- Balanced fast-field echo
- Acq. speed: 333 ms/frame
- 1-minute continuous scanning

2D dMRI review: Feng et al. IJROBP 2009; 74 (3): 884

Diaphragm: good (rare) ***poor (common)***



Abdo. wall: good (rare) ***poor (common)***

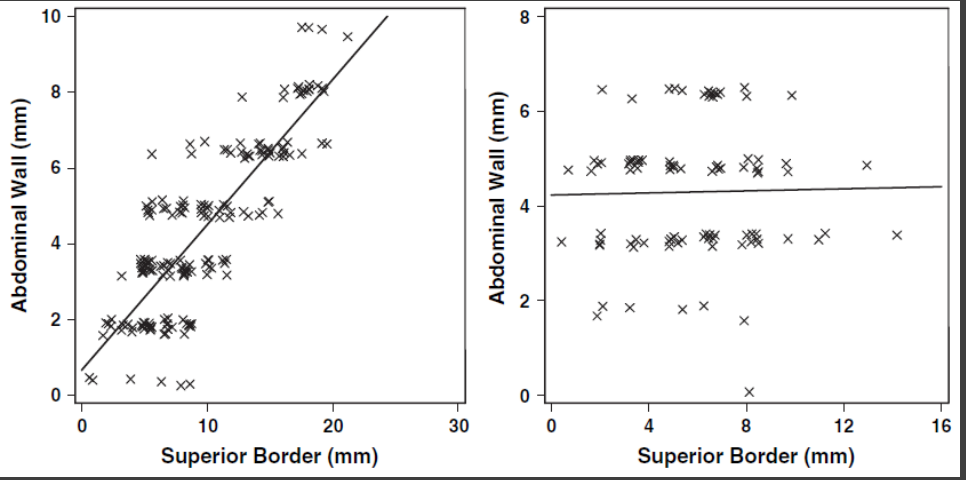


Table 4. Sensitivity, specificity, and accuracy of gating based on 10% range of tumor motion between exhale and inhale for various potential surrogates for the position of the inferior tumor border

Feature	Sensitivity	Specificity	Accuracy
Abdominal wall	57	63	62
Diaphragm	53	68	65

Sensitivity: % of time beam was on when it should have been (tumor coverage)
Specificity: % of time beam was off when it should have been (normal tissue sparing)
Accuracy: % of time that both surrogate and tumor were in 10% range of motion gating window simultaneously

Conclusions:

- Pancreatic tumor motion is complex with high inter-subject variability
- Significant tumor deformation observed
- Abdominal wall and diaphragm are poor surrogates for tumor motion

II. Review of selection of 2D dynamic MRI studies:

1. Lung: Koch et al. [IJROBP 2004; 60 (5): 1459]
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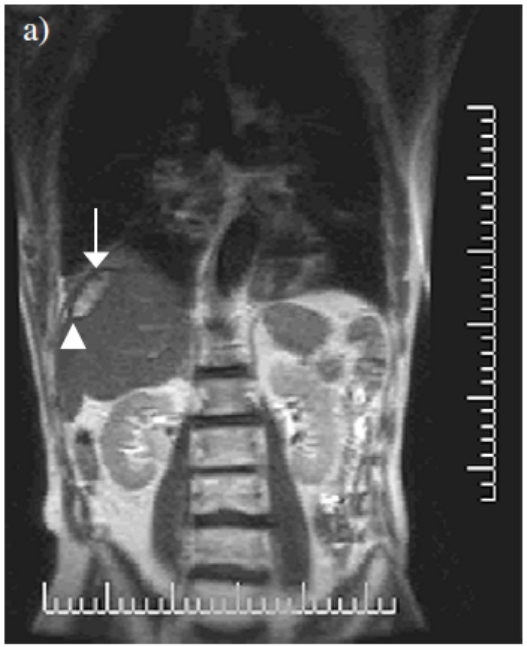
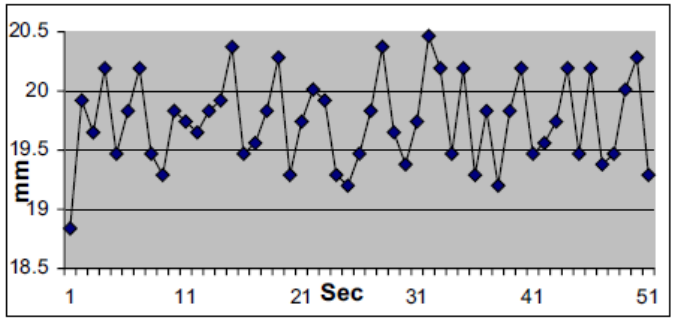
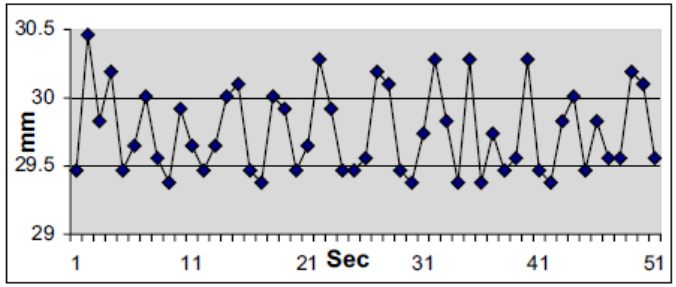
3. **Liver: Kirilova et al. [IJROBP 2008; 71 (4): 1189]**
4. Lung: Cai et al. [PMB 2007; 52: 365]
   [IJROBP 2007; 60(3): 895]

2D dMRI review: Kirilova et al. IJROBP 2008; 71 (4): 1189

- Study in 36 (primary and metastatic) liver SBRT patients
- Patients underwent 60 second flouro. to observe SI motion of diaphragm
- On same day, 2D dMRI in axial, sag and coronal planes to measure tumor motion
- Simple analyses of maximal tumor and diaphragmatic excursions







- 1.5 T (GE Signa)
- T_2 single-shot fast spin echo sequence
- TR: 1300 ms; TE: 90 ms
- Pixel size: 1.6^2-2.5^2 mm^2
- Slab thickness: 5 mm
- Acq. speed: 1 frame/sec.
- 60 seconds continuous acquisition

2D dMRI review: Kirilova et al. IJROBP 2008; 71 (4): 1189

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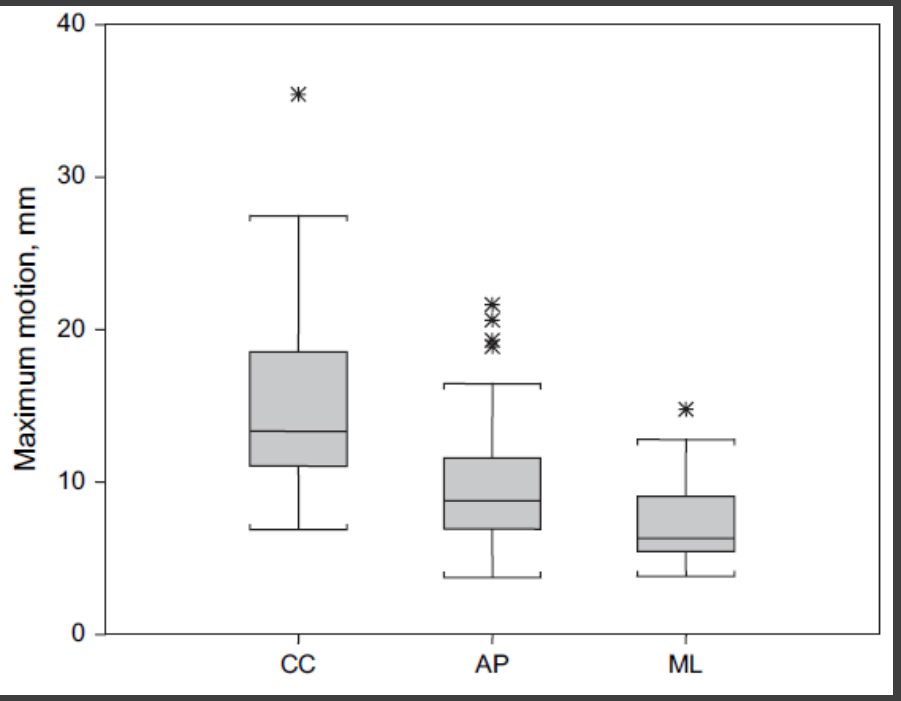
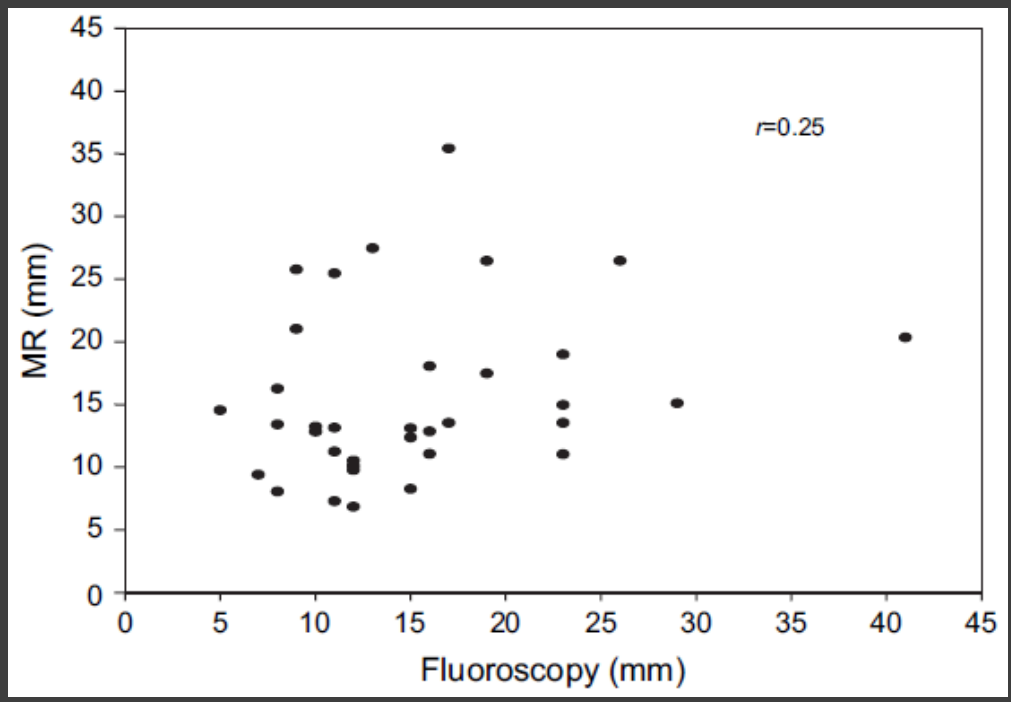
Max. tumor excursion on dMRI



Max. diaphragm excursion on flouro.



Conclusions:

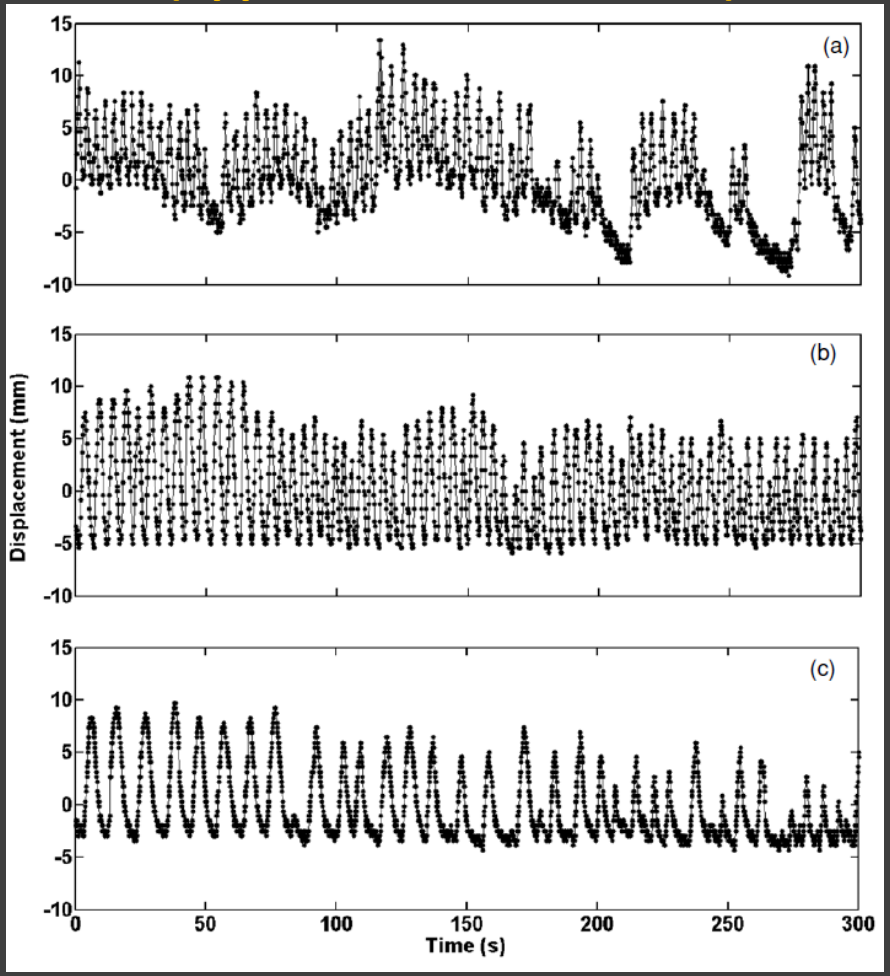
- dMRI for radiotherapy is both feasible and non-invasive
- SI tumor motion (maximum amplitude) not well correlated with SI diaphragm motion (maximum amplitude)

II. Review of selection of 2D dynamic MRI studies:

1. Lung: Koch et al. [IJROBP 2004; 60 (5): 1459]
2. Pancreas: Feng et al. [IJROBP 2009; 74 (3): 884]
3. Liver: Kirilova et al. [IJROBP 2008; 71 (4): 1189]
4. **Lung: Cai et al. [PMB 2007; 52: 365]**
   [IJROBP 2007; 60(3): 895]

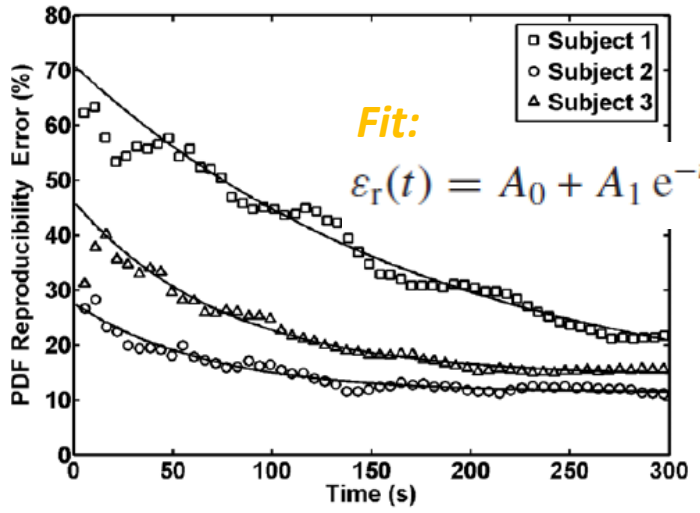
2D dMRI review: Cai et al. PMB 2007; 52: 365

- 2D dMRI thoracic study in 3 volunteers
- Purpose was to examine (tumor) PDF stability/reproducibility given the potential application of the PDF in 4D RTP
- Scanned in sagittal plane at baseline and 2-3 weeks later
- 3 vessels (upper, middle and lower) tracked per subject



- 1.5 T (Siemens Sonata)
- TrueFISP ("True Fast Imaging with Steady-State Precession," aka, balanced steady-state free precession – bSSFP).
- TR: 105 ms; TE: 0.93 ms
- Flip angle: 52 degrees
- Pixel size: ≈2.6 × 1.7 mm^2
- Slice profile (~thickness): 7 mm
- Acq. speed: ≈ 10 frames/sec.
- 5 minutes continuous acquisition
- Cross-correlation based tracking
- Images up-sampled 5× for better tracking accuracy

2D dMRI review: Cai et al. PMB 2007; 52: 365



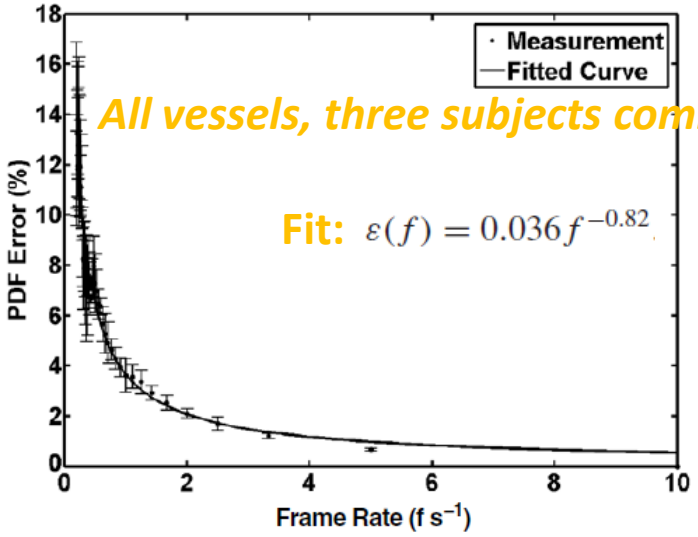
Fit:

$$\varepsilon_r(t) = A_0 + A_1\, e^{-t/A_2}$$

Figure 3. Absolute PDF reproducibility errors plotted as a function of MR scan time for each of the subjects. Measurement data are the mean over the three tracked lung vessels.

PDF Reproducibility Error:

$$\varepsilon_r(t) = \frac{\int |\mathrm{PDF}_2(\delta, t, 10) - \mathrm{PDF}_1(\delta, t, 10)|\, d\delta}{2} \times 100\%.$$



All vessels, three subjects combined

Fit: $\varepsilon(f) = 0.036 f^{-0.82}$

Figure 4. Absolute PDF error plotted as a function of the imaging frame rate. Data are the average over all the tracked pulmonary vessels.

PDF Reproducibility Error as a function of frame rate:

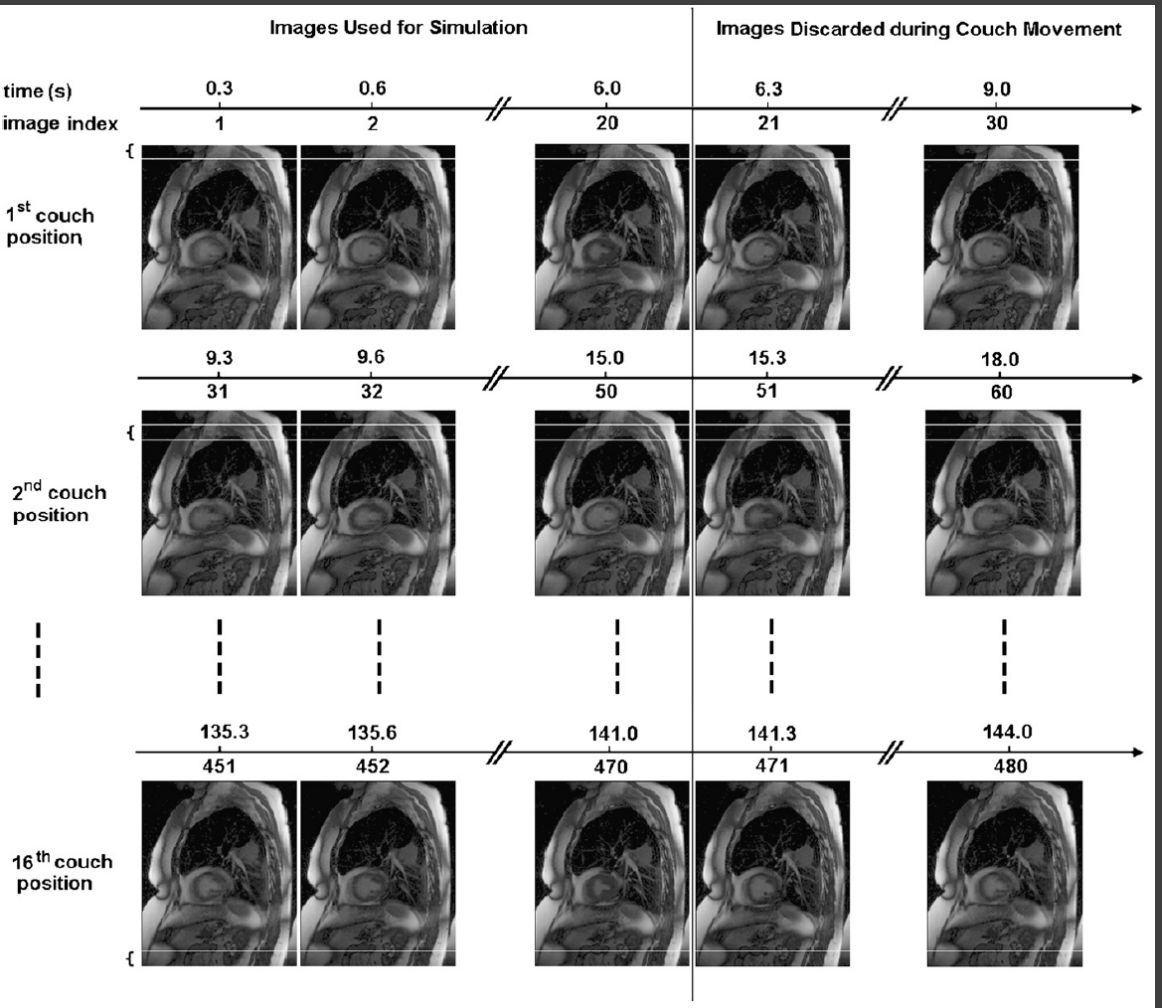
$$\varepsilon(f) = \frac{\int |\mathrm{PDF}(\delta, 300, f) - \mathrm{PDF}(\delta, 300, 10)|\, d\delta}{2} \times 100\%$$

Conclusions:

- Derived PDF not simply patient-dependent, but is also dependent on study time and frame rate.
- Derived PDF less dependent on frame rate than on scan time

2D dMRI review: Cai et al. IJROBP 2007; 60(3): 895

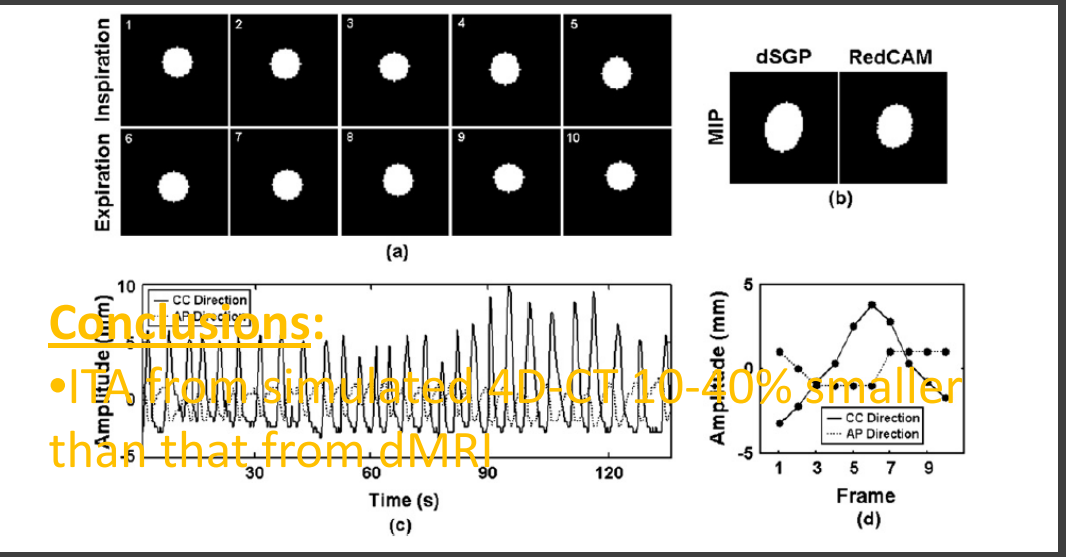
- 2D dMRI study in 6 lung cancer patients and 8 healthy volunteers
- Sagittal scanning in a single slice for 5 minutes continuously
- 2D MIPs from full dMRI study were compared to derived 2D Internal Target Areas (ITA) for simulated cine-mode 4D-CT study
- Respiratory signal for "4D-CT" sorting was the tumor (patients) or a tracked vessel (volunteers)



- 1.5 T (Siemens Avanto)
- TrueFISP (or bSSFP) sequence
- TR: 105 ms; TE: 0.93 ms
- Flip angle: 52 degrees
- Pixel size: 1.5^2 mm^2
- Slice profile (~thickness): 7 mm
- Acq. speed: 3.33 frames/sec.
- 5 minutes continuous acquisition

2D dMRI review: Cai et al. IJROBP 2007; 60(3): 895

Volunteers assuming 24 mm (diam.) circular tumor:



Conclusions:

- ITA from simulated 4D-CT 10-40% smaller than that from dMRI
- Clear dependency of ITA on breathing variability

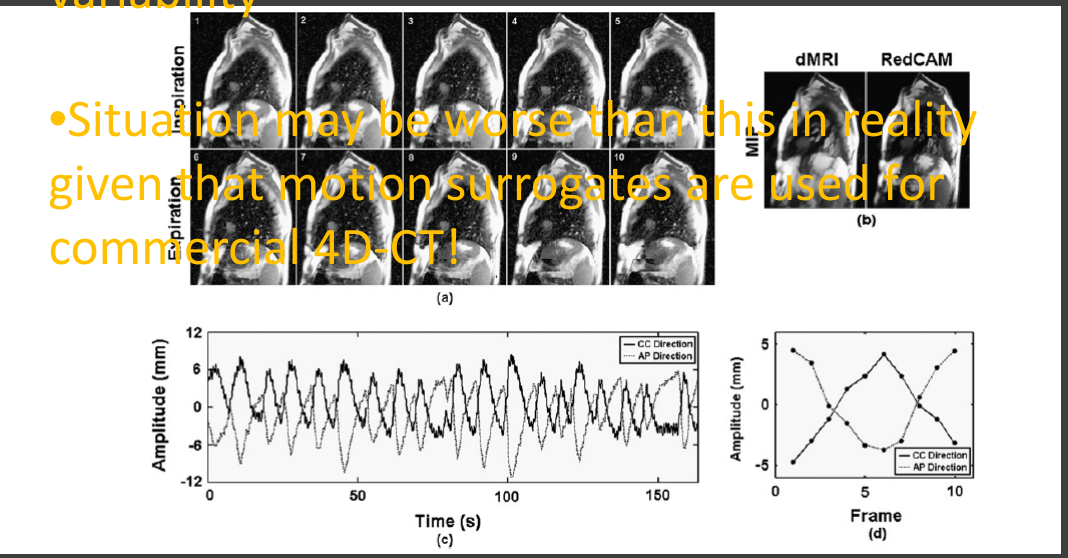
Internal Target Area Error:

$$\epsilon = \frac{ITA_{RedCAM} - ITA_{dSGP}}{ITA_{dSGP}} \times 100\%$$

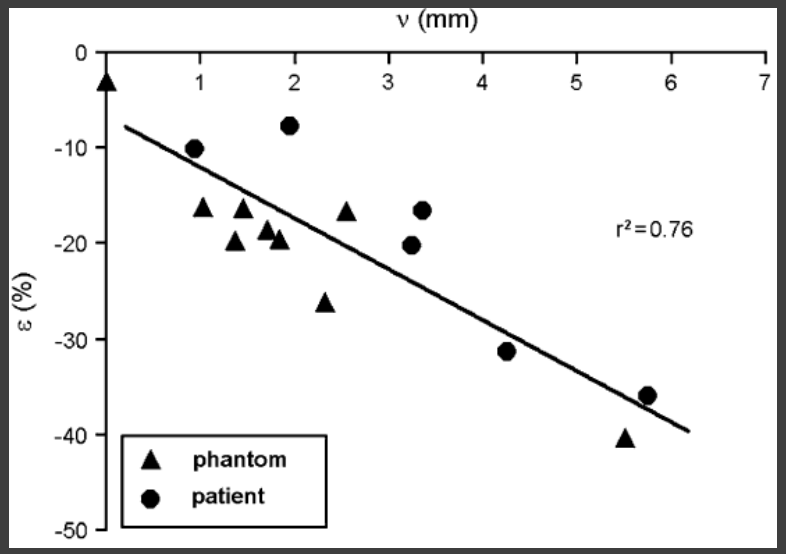
Breathing Variability from tracked motion trajectory:

$$\nu = \frac{STD(peaks) + STD(valleys)}{2}$$

Patients:



- Situation may be worse than this in reality given that motion surrogates are used for commercial 4D-CT!



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III. Review selected studies where "4D-MRI" is derived using 2D slice-stacking:

1. Liver: von Siebenthal et al. [PMB 2007; 52: 1547]

2. Lung: Cai et al. [Med. Phys. 2011; 38 (12): 6384]

3D dMRI review: von Siebenthal et al. PMB 2007; 52: 1547

- **Multi-slice abdominal 2D dMRI study in volunteers demonstrating principle of navigator slice-based retrospective sorting to derive a "4D-MRI"**

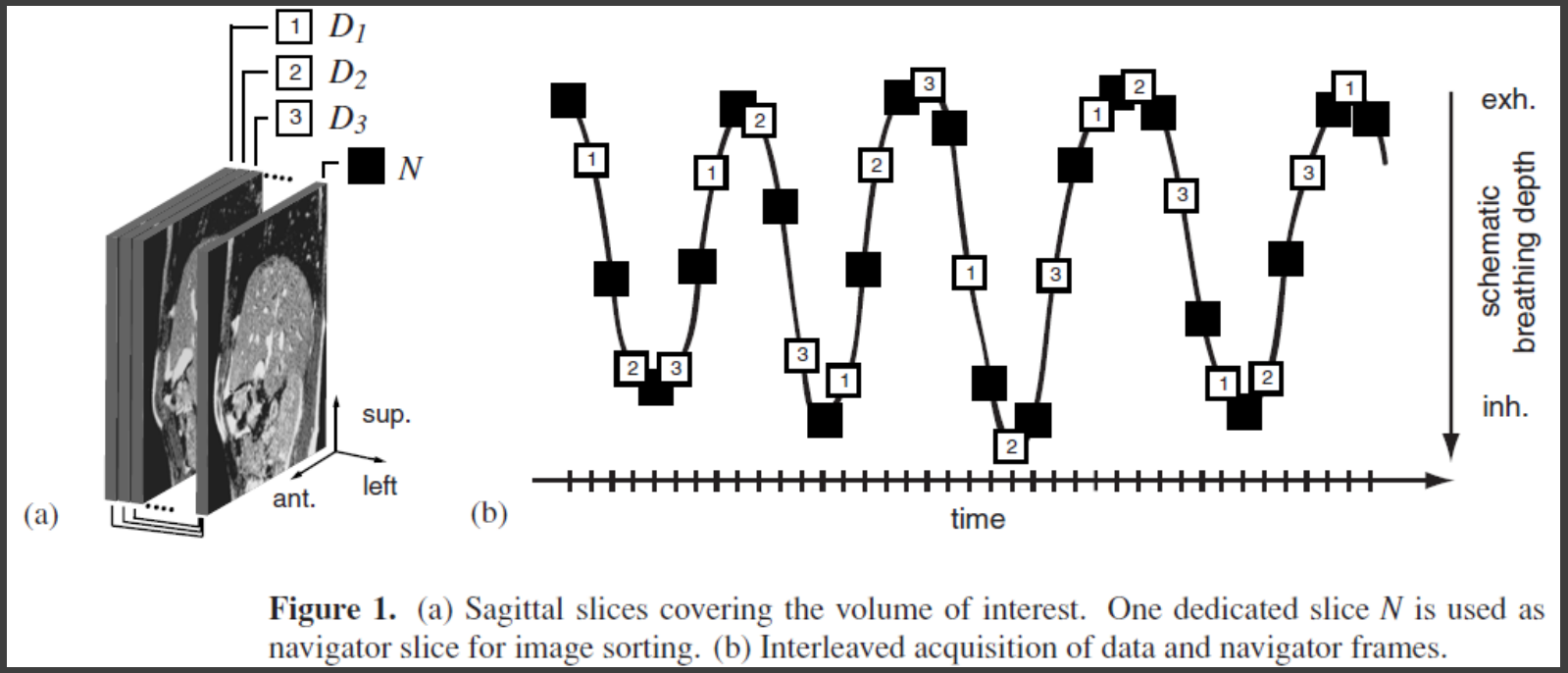
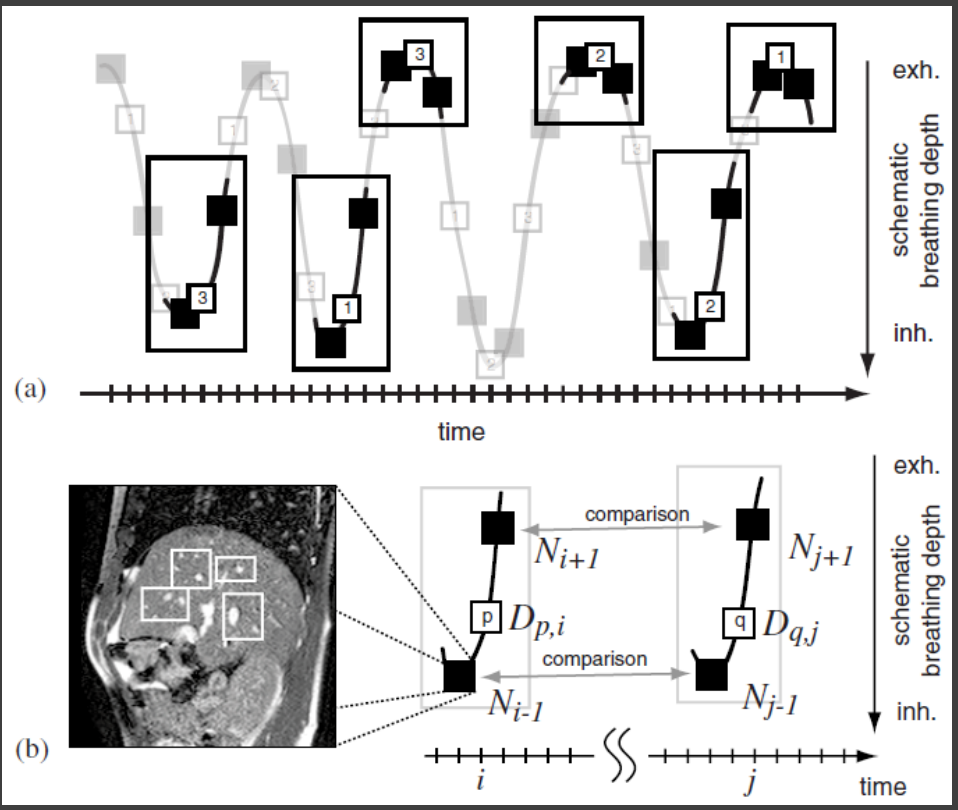


Figure 1. (a) Sagittal slices covering the volume of interest. One dedicated slice *N* is used as navigator slice for image sorting. (b) Interleaved acquisition of data and navigator frames.

- 1.5 T (Philips Achieva)
- Steady-State Free Precession
- TR: 3.1 ms
- Flip angle: 70 degrees
- Pixel size: 1.8^2 mm^2
- Slice profile (~thickness): 3-4 mm
- Acq. speed: 5.3-5.6 frames/sec.
  → Effective acq. speed: 2.6-2.8 frames/sec.
- Sequential sagittal slice acquisition (with 22-30 slices)
- Continuous acquisition over tens of minutes

3D dMRI review: von Siebenthal et al. PMB 2007; 52: 1547



Cost function:

combines template-matching derived shifts from navigator sub-regions

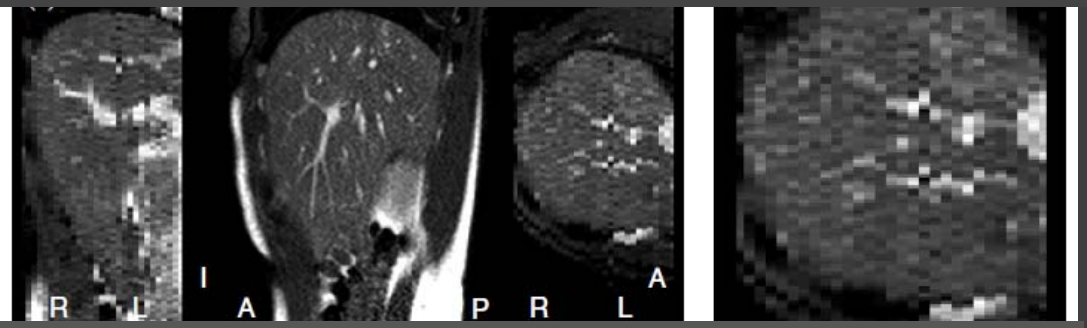
$$c(i,j) = \sum_{r=1}^{P} \left\| \begin{pmatrix} x^r_{j-1} - x^r_{i-1} \\ y^r_{j-1} - y^r_{i-1} \end{pmatrix} + \begin{pmatrix} x^r_{j+1} - x^r_{i+1} \\ y^r_{j+1} - y^r_{i+1} \end{pmatrix} \right\|$$

$$= \sum_{r=1}^{P} \left\| \Delta \vec{X}^r_{-1} + \Delta \vec{X}^r_{+1} \right\|.$$

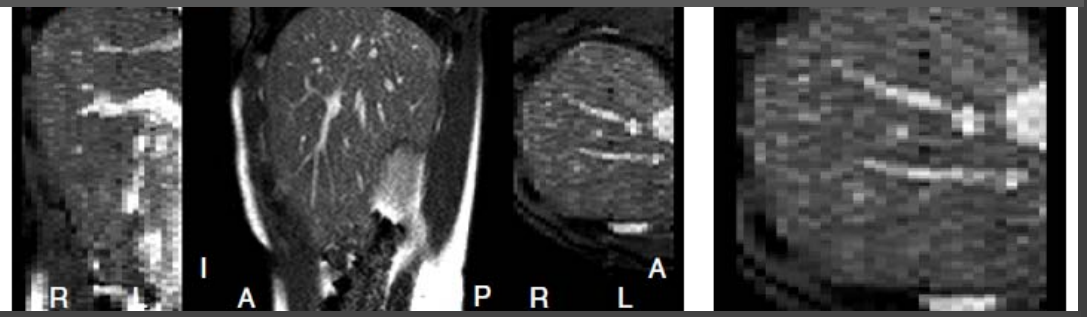
Each pair of consecutive or "embracing" navigator frames defines a liver "state" for sorting from which an entire 3D volume can be reconstructed.

3D dMRI review: von Siebenthal et al. PMB 2007; 52: 1547

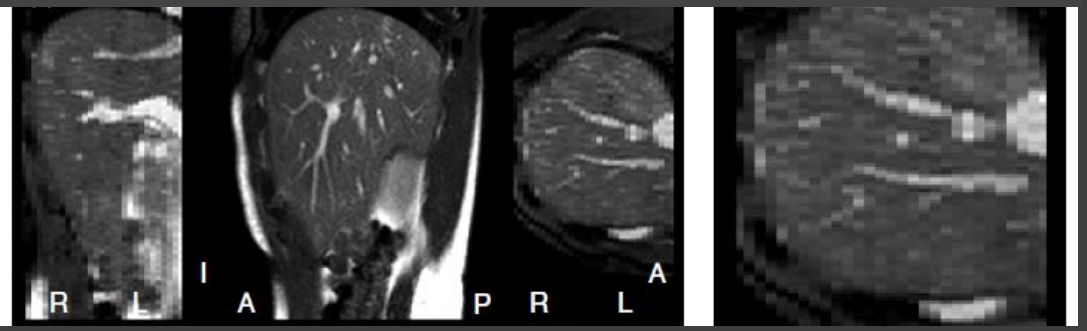
Simple navigator sorting based on 1D diaphragm



Proposed sorting method



Proposed method averaging over 5 best matching frames



Potential drawbacks:

- The dependency on the navigator may prolong the study

Conclusions:

- Relatively complex image processing
- Provides a means for deriving high-quality "4D-MRI" for RTP that specifically addresses breathing motion variability
- If the goal is to derive a representative "4D-MRI" for planning (e.g., single-cycle 3D anatomic movie, as in 4D-CT), how does one define the set of reference navigator states?
- One can simulate continuous/real-time 3D anatomic motion over the full imaged duration (at frame rate of navigator frames)
- Surrogates for sorting have no direct extension to potential surrogates used for guidance of the therapy

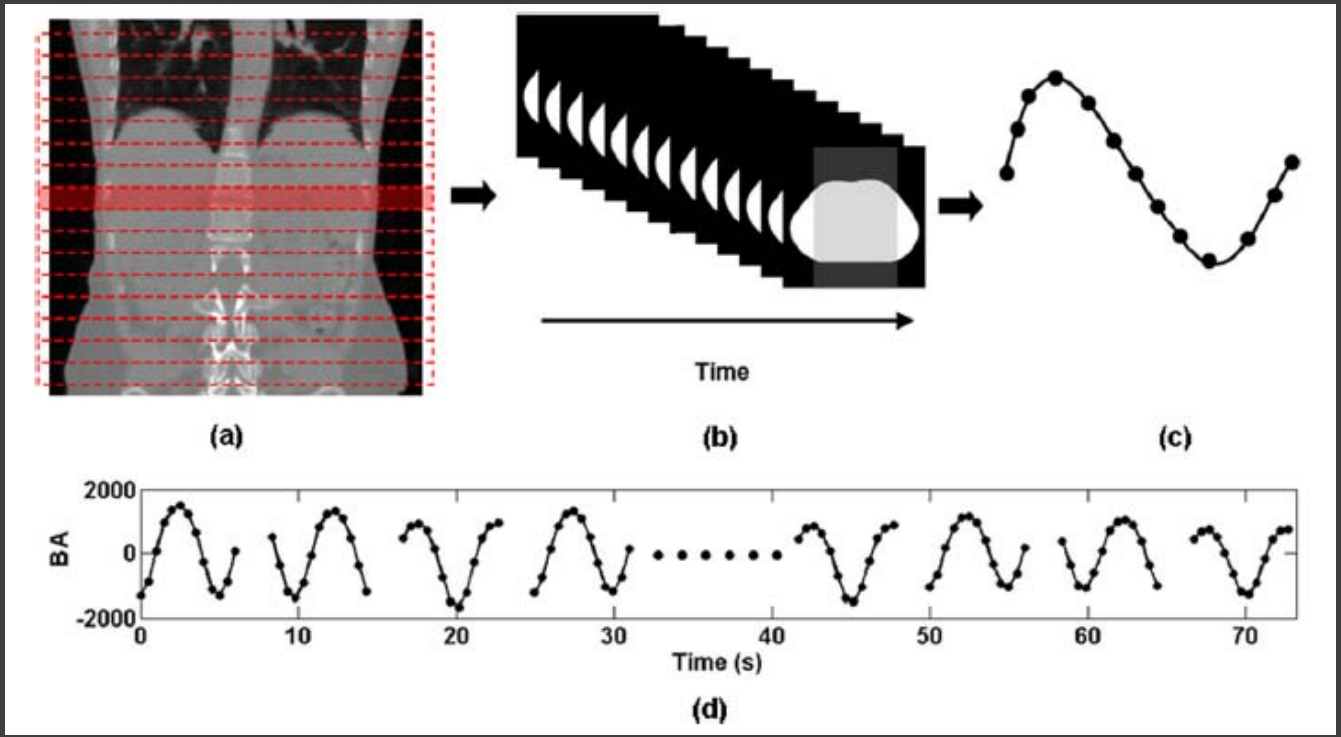
III. Review selected studies where "4D-MRI" is derived using 2D slice-stacking:

1. Liver: von Siebenthal et al. [PMB 2007; 52: 1547]

2. Lung: Cai et al. [Med. Phys. 2011; 38 (12): 6384]

3D dMRI review: Cai et al. Med. Phys. 2011; 38 (12): 6384

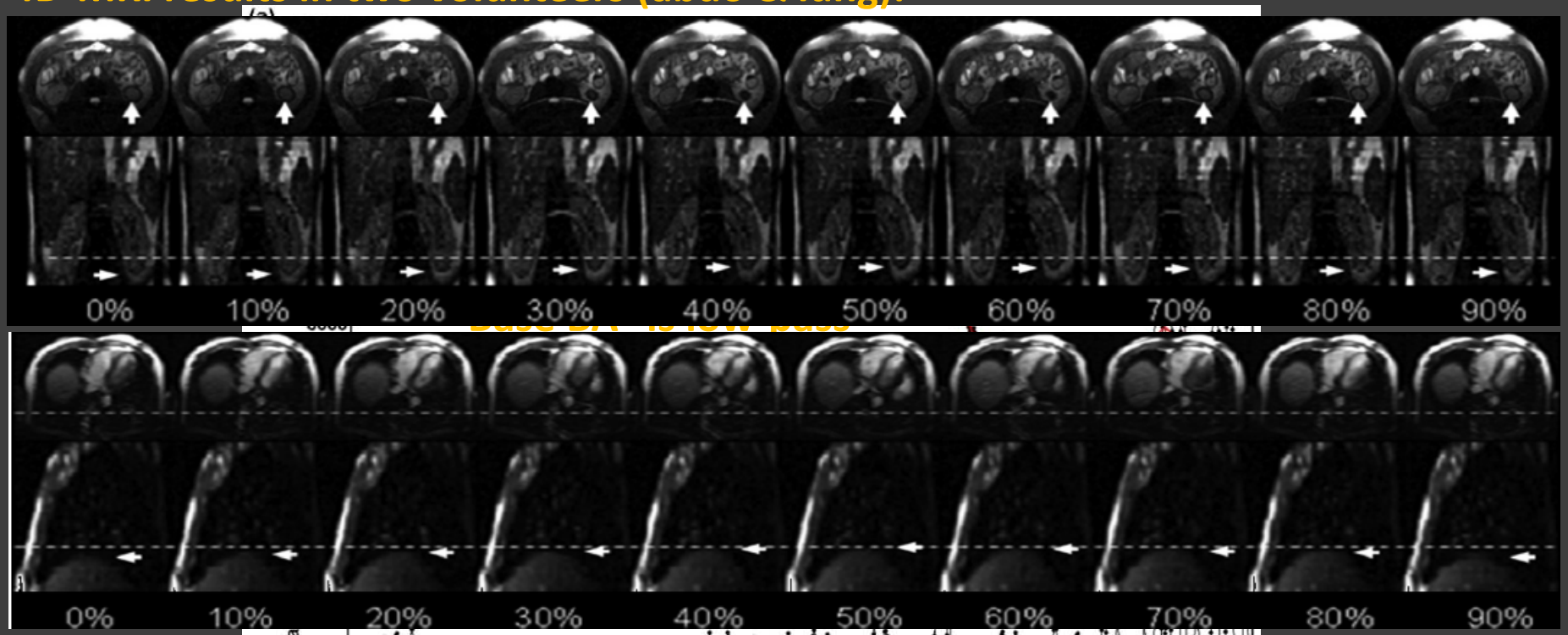
- Comprehensive patient, phantom and volunteer study demonstrating feasibility of practical acquisition and sorting technique for representative "4D-MRI"
- 2D dMRI acquired axially – slice location incremented every ave. resp. period + 1 sec.
- Respiratory surrogate for sorting is image-based "Body Area" (BA)
- This surrogate first validated with 4D-CT data/images in patients

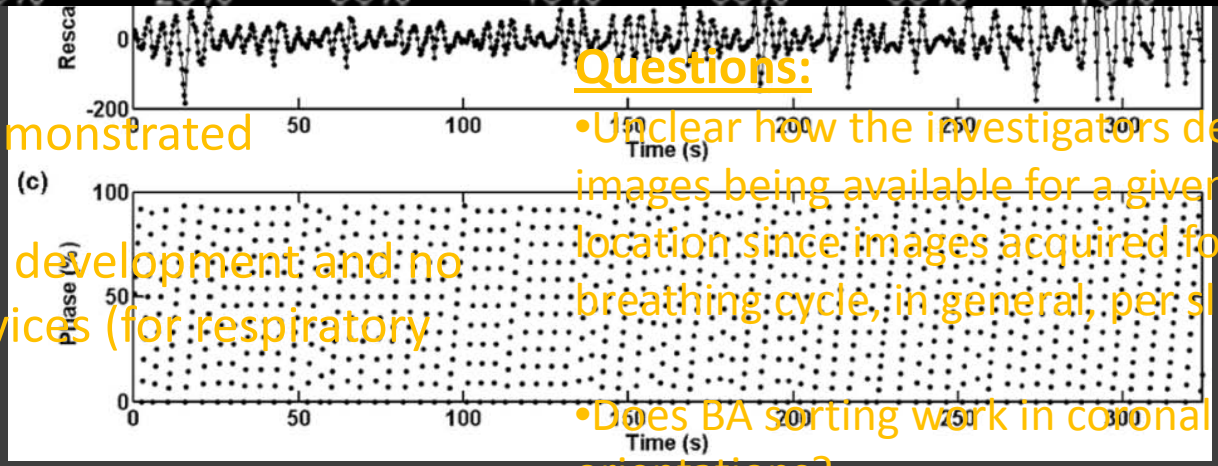


- Siemens Avanto (1.5 T)
- TrueFISP (bSSFP)
- TR: 3.6 ms; TE: 3.7 ms
- Pixel size: ≈1.4^2 mm^2

3D dMRI review: Cai et al. Med. Phys. 2011; 38 (12): 6384

4D-MRI results in two volunteers (abdo & lung):





Conclusions:

- Feasibility demonstrated
- No sequence development and no additional devices (for respiratory surrogate)

Questions:

- Unclear how the investigators deal with multiple images being available for a given phase and slice location since images acquired for longer than one breathing cycle, in general, per slice
- Does BA sorting work in coronal and sagittal orientations?

IV. 4D-MRI methods development at Johns Hopkins:

<u>Method 1</u>: 2D-to-4D sorting of dMRI to derive a representation of the subjects' average breathing cycle

<u>Method 2</u>: 4D tumor tracking using orthogonal 2D dMRI slice planes

IRB-approved methods development study in volunteers underway

<u>Collaborators:</u>

Teboh Roland, Ph.D.
Russell Hales, M.D.
Todd McNutt, Ph.D
Joseph Herman, M.D.
John Wong, Ph.D.

Project receives personnel support from Siemens:

Steven Shea, Ph.D.
Aaron Flammang, Ph.D.

SIEMENS

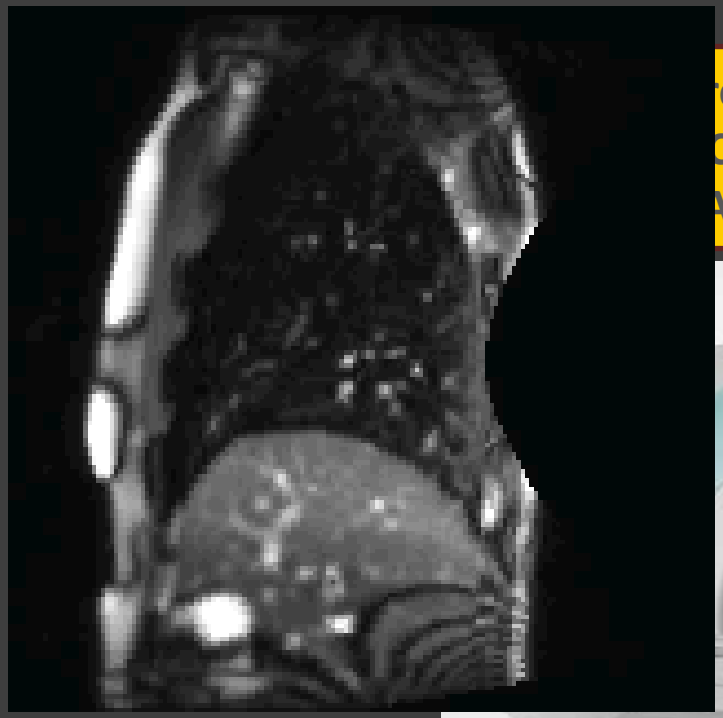
JHU method 1:

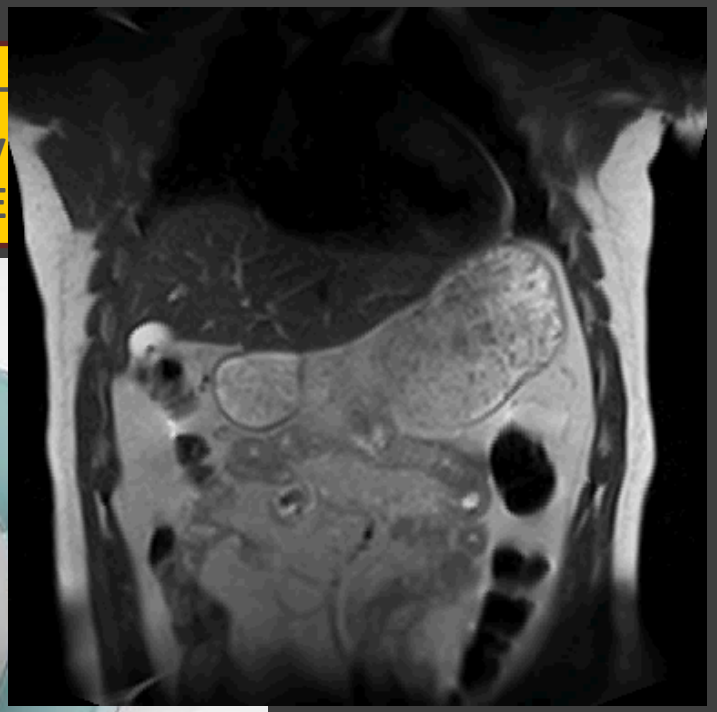
Goals:

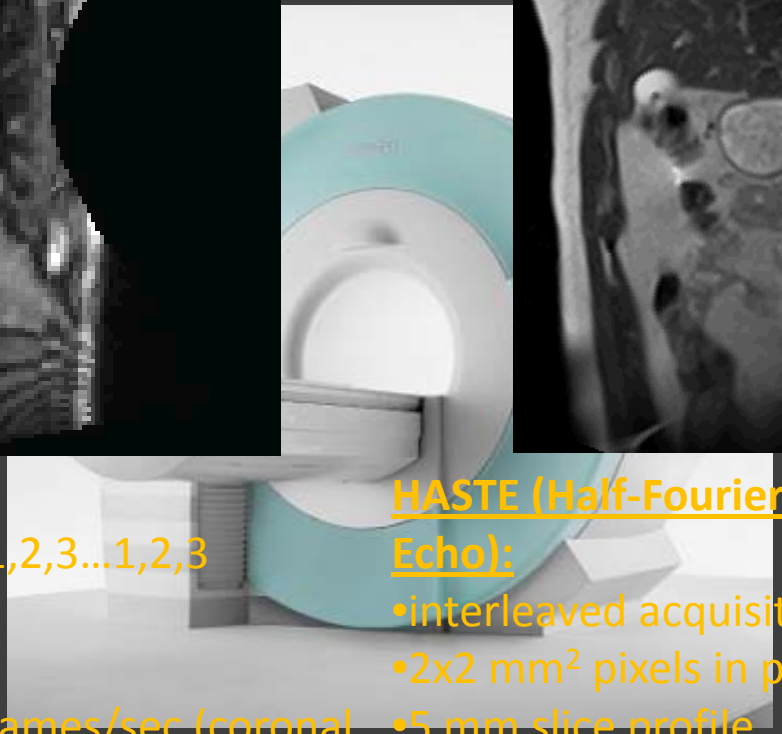
- With clinical workflow and practicality in mind, develop methods to derive a robust, representative "4D-MRI" for direct application to RTP similar to present utility of 4D-CT

- This "4D-MRI" method should, in particular, address problems associated with variable breathing

JHU method 1: image acquisition







TrueFISP (or bSSFP):

- stepped acquisition (slice 1,2,3…1,2,3
- 2x2 mm^2 pixels in plane
- 5 mm slice profile
- acquisition speed: 4 to 5 frames/sec (coronal and sagittal, respectively
- strong blood signal w/o contrast on board

HASTE (Half-Fourier Single-Shot Turbo Spin Echo):

- interleaved acquisition (slice 2,4,6…1,3,5…)
- 2x2 mm^2 pixels in plane
- 5 mm slice profile
- acquisition speed: 2.85 – 3.33 frames/sec. (coronal and sagittal respectively)
- strong fat signal; good abdominal contrast

JHU method 1: simultaneous respiratory monitoring

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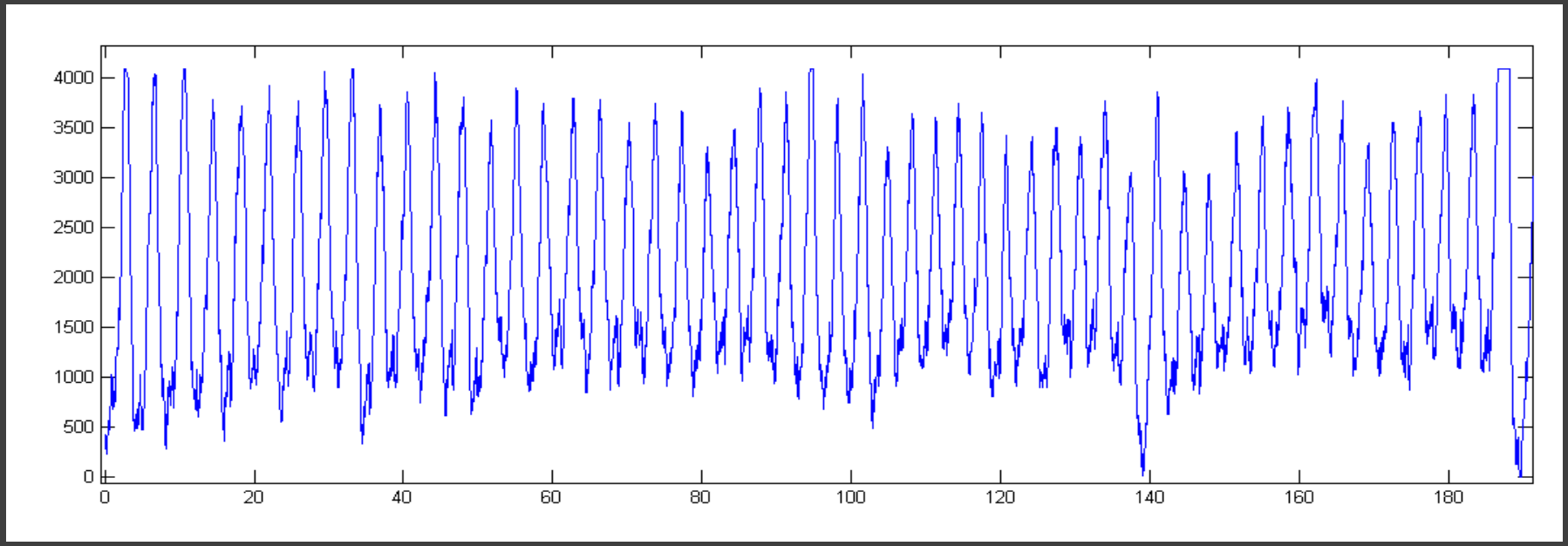
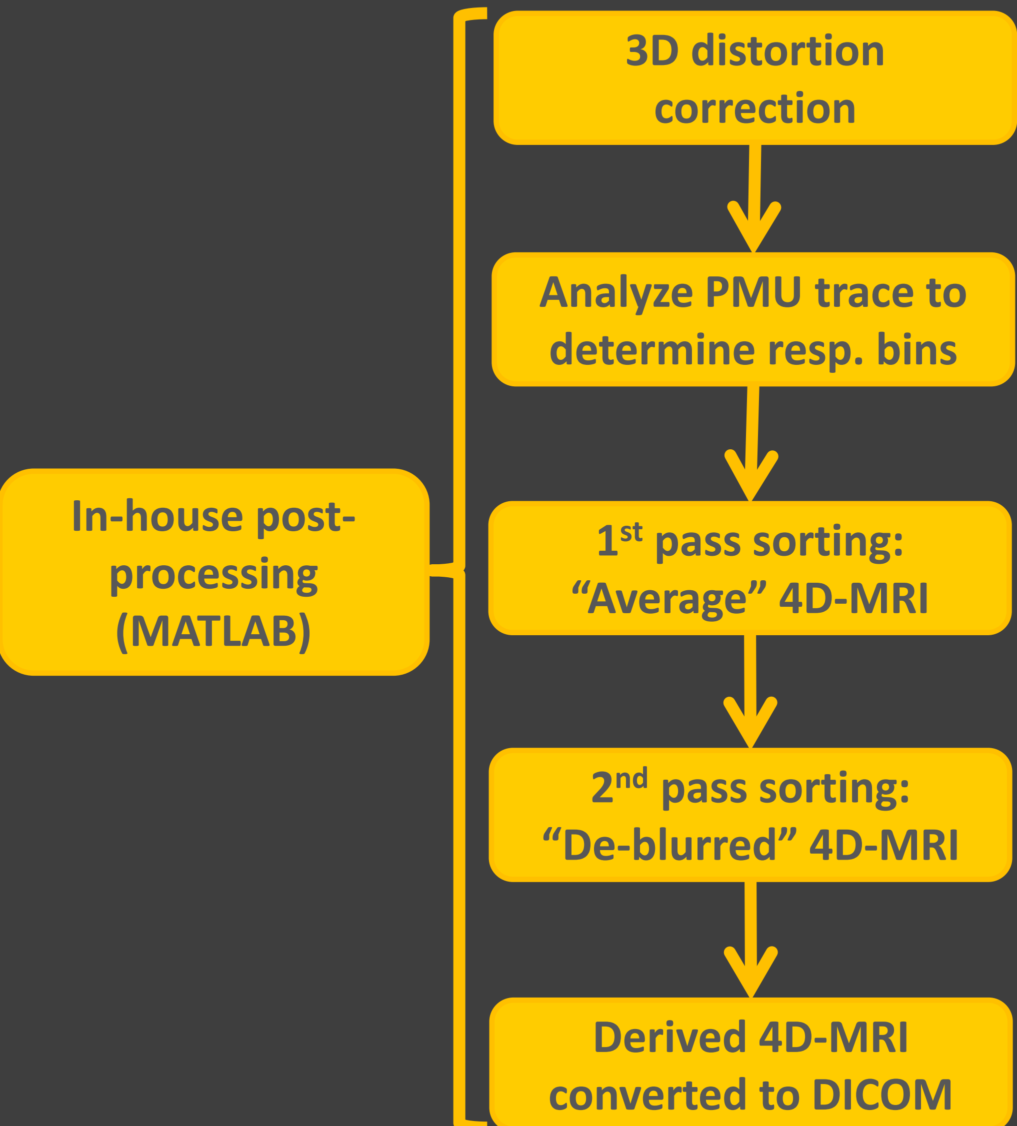
Acquire external respiratory signal (Physiological Monitoring Unit -- PMU)



PMU logging:

- synchronized with the image acquisition computer (well, in principle, anyway)
- auto started/stopped within sequence run
- sampled at ~50 Hz

JHU method 1: post-processing



1st-pass Sorting:

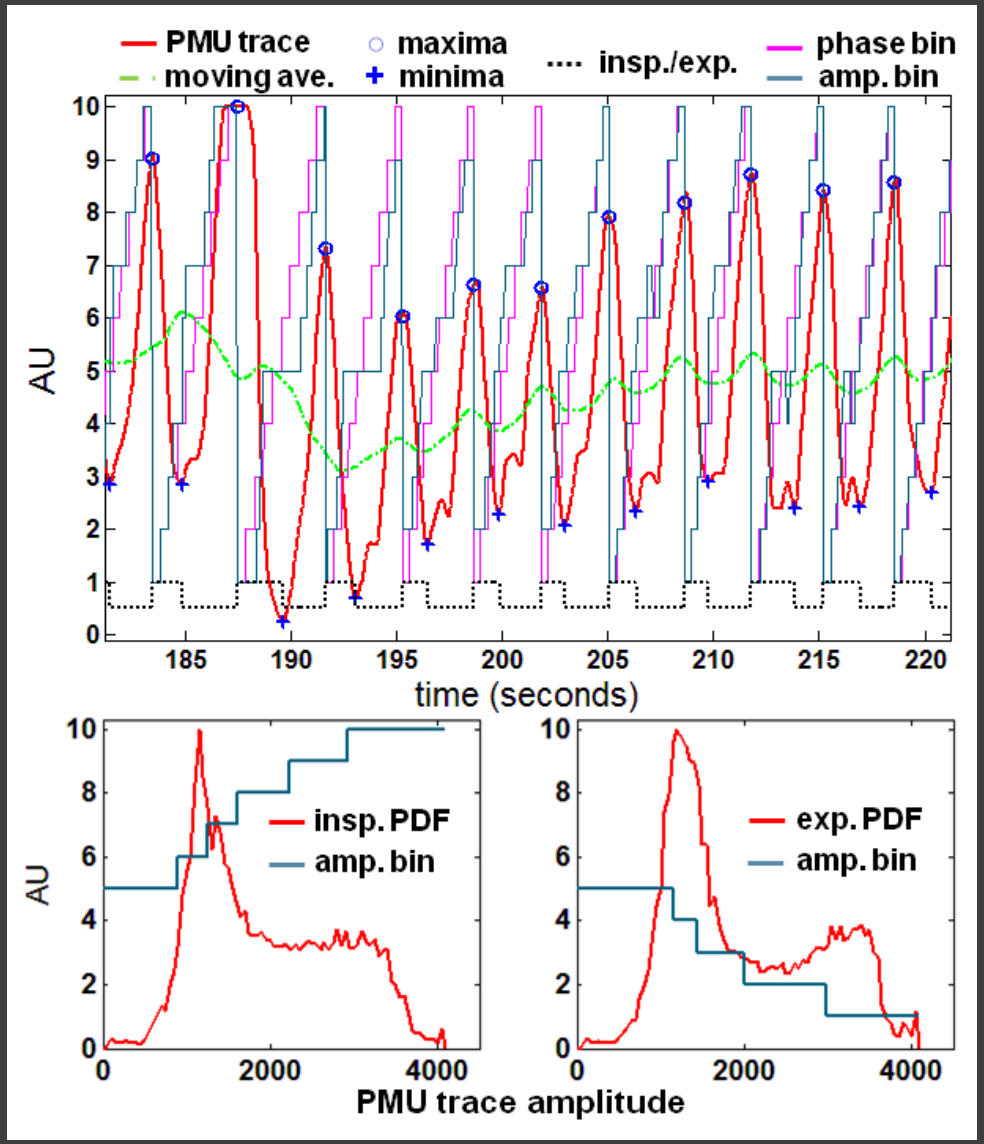
- Retrospective "slice stacking" employed
- Raw frames, per slice location, assigned to 3D recon associated with PMU respiratory bins (up to ~15 bins)
- Each bin of given slice location is an average image over all available frames
- Corresponding standard deviation image computed

2nd-pass Sorting:

- Each raw frame compared with 1st-pass result for corresponding slice across all respiratory bins (within rectangular 2D template region)
- 2D normalized cross-correlation-based comparison/selection (user-defined rectangular ROI) of (N) best matching raw frames
- Only these N frames per slice location and respiratory bin are used for 2nd recon

JHU method 1:

Analysis of PMU surrogate to determine respiratory intervals

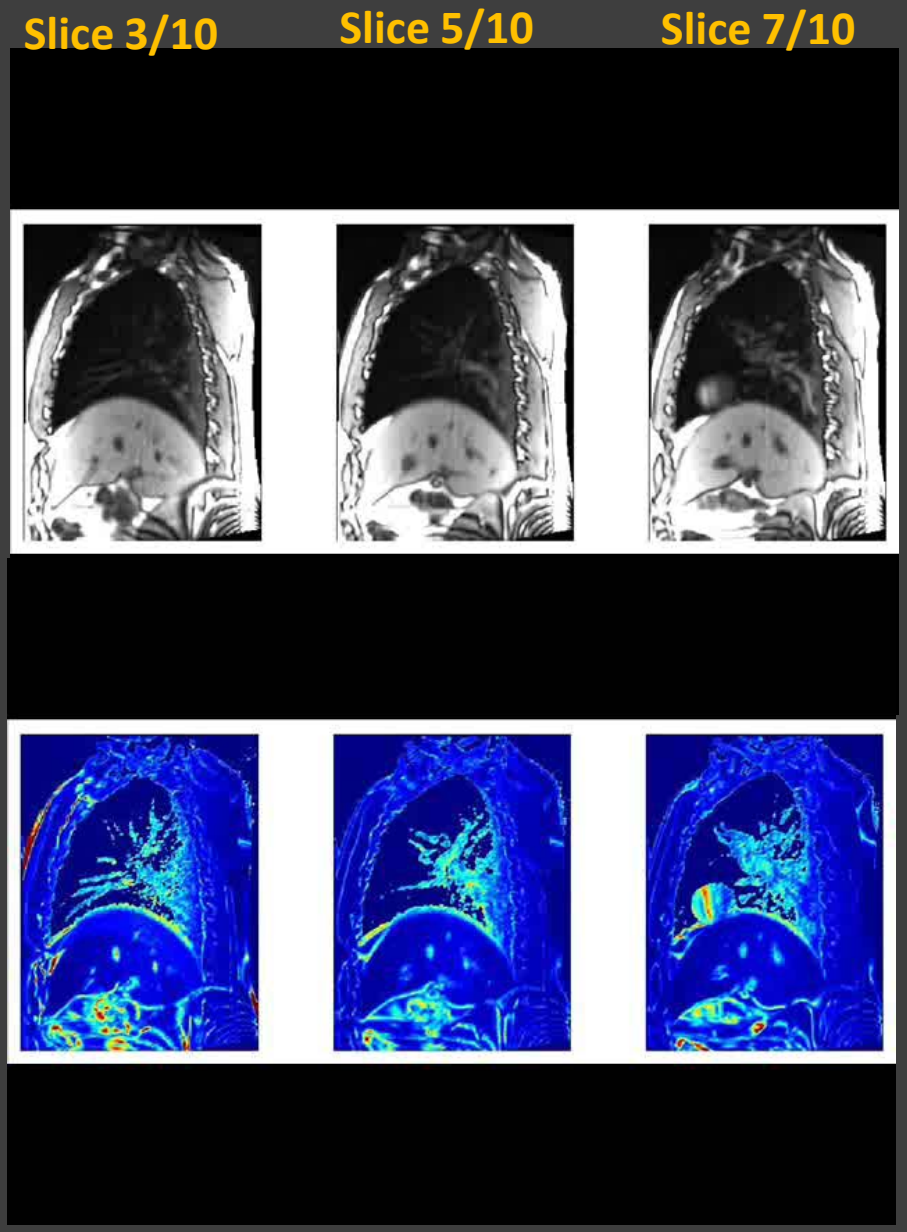


- The "Moving Average" [Lu et al., Med Phys. 2006; 33 (10)] is quantified to aid in identification of maxima/minima.

- Amplitude binning is based on "Amplitude Probability" which is being explored to potentially improve the first-pass sorting.

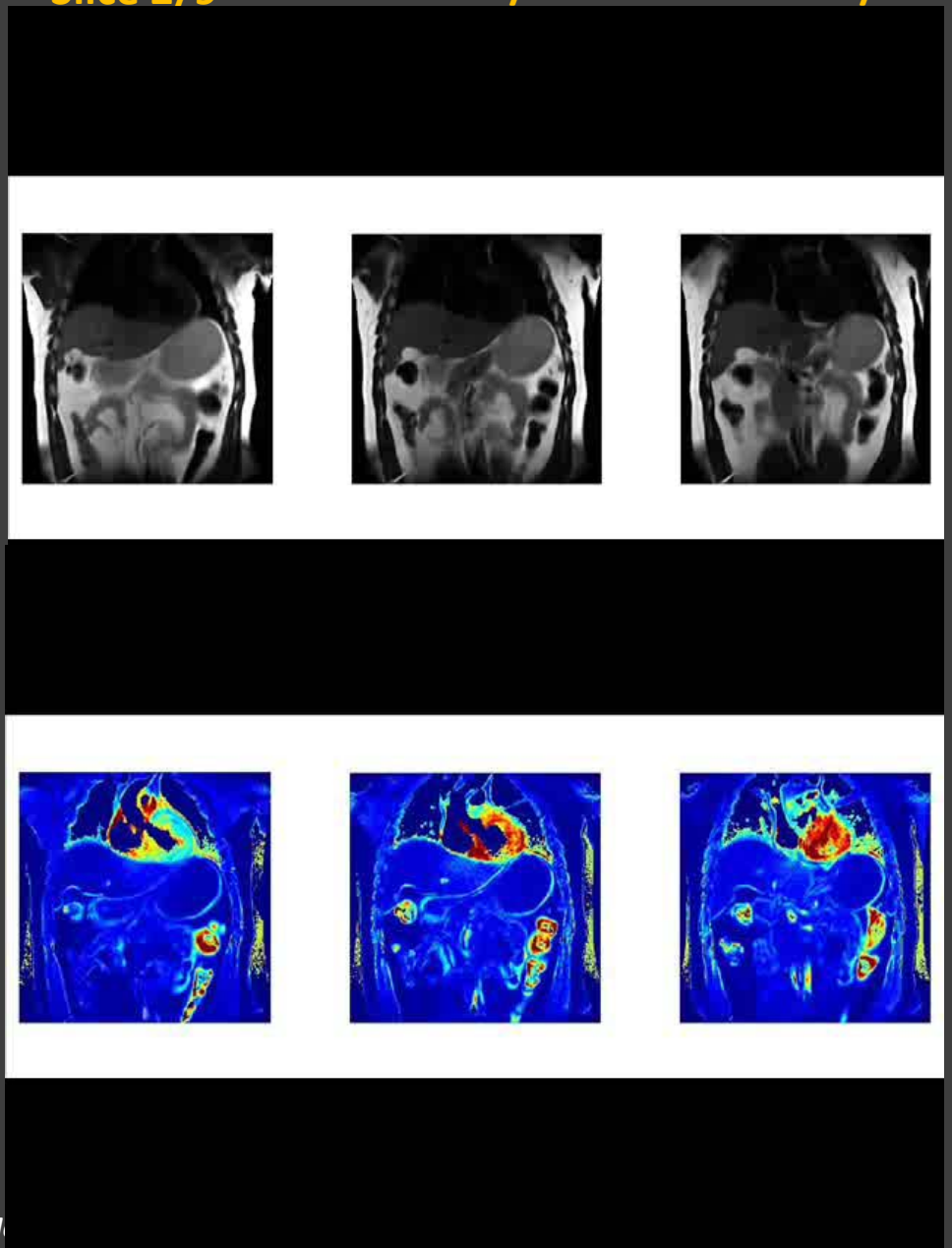
Note: this method is an adaptation of that presented by Olsen et al. [IJROBP 2008; 70 (1): 243]

JHU method 1: Results for 1st-pass reconstruction



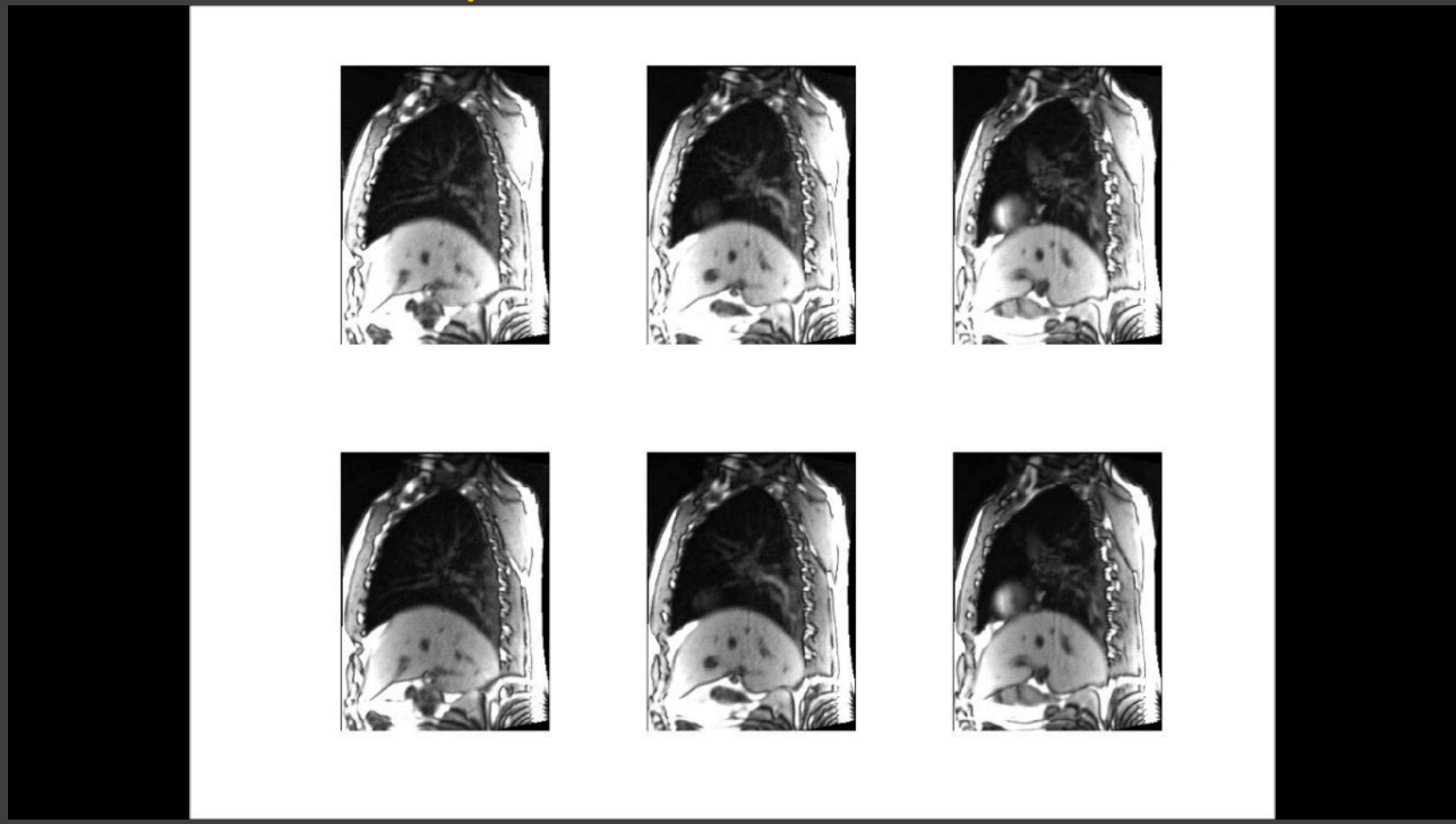
- bSSFP in lung volunteer (dark blood pulse on)
- 10-phase-bin reconstruction
- Average frames/bin/slice = 17

JHU method 1: Results for 1st-pass reconstruction



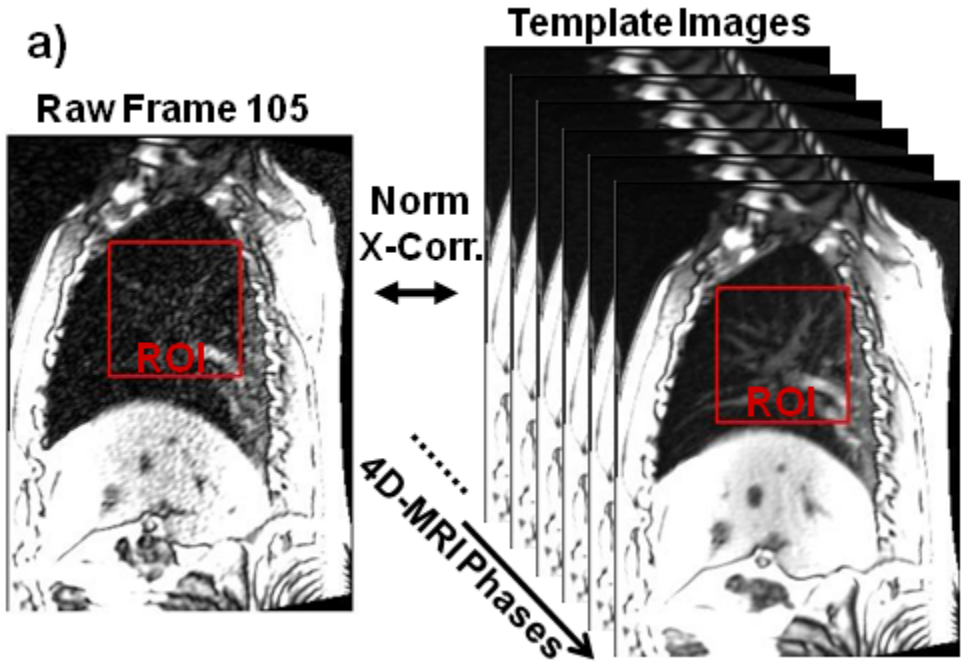
- HASTE in abdo volunteer
- 10-phase-bin reconstructio
- Average frames/bin/slice = 26

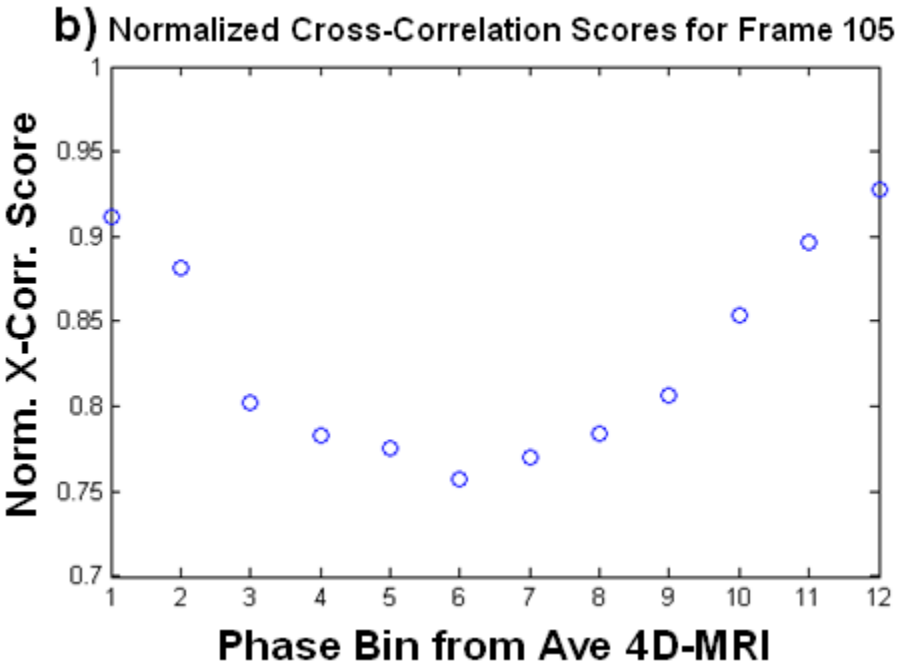
JHU method 1:
1st pass result for amplitude-probability vs. phase binning



JHU method 1:

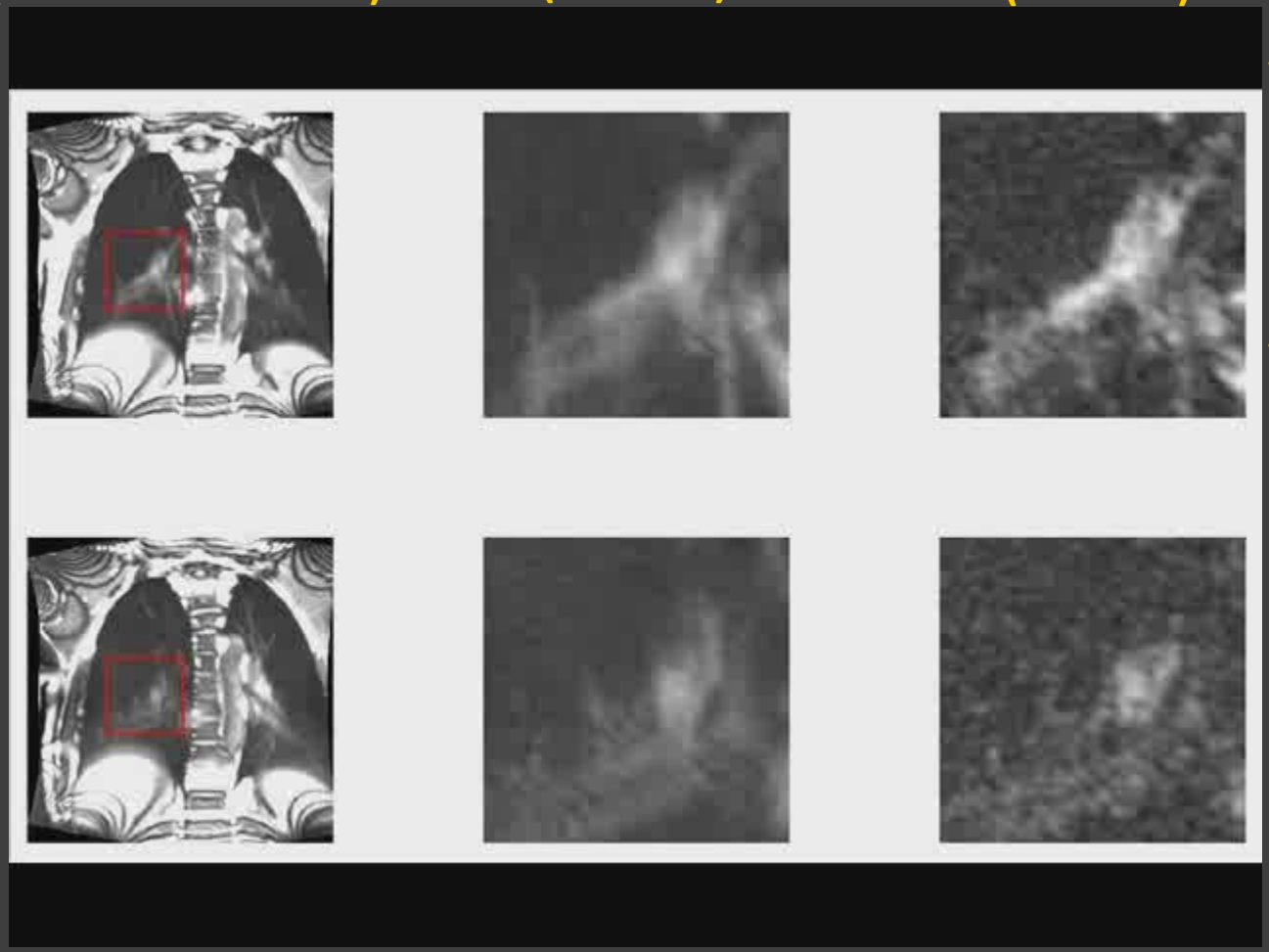
Normalized cross-correlation based scoring to determine best maching frames for 2nd pass reconstruction





- Clear indication of best matching phase (despite poor SNR in raw image in this case)

JHU method 1: Results for 2nd-pass reconstruction



- bSSFP in lung volunteer (dark blood pulse on)
- Subject imaged for 30 minutes continuously
- 1st- Pass result derived from respiratory phase binning
- 10-phase reconstruction

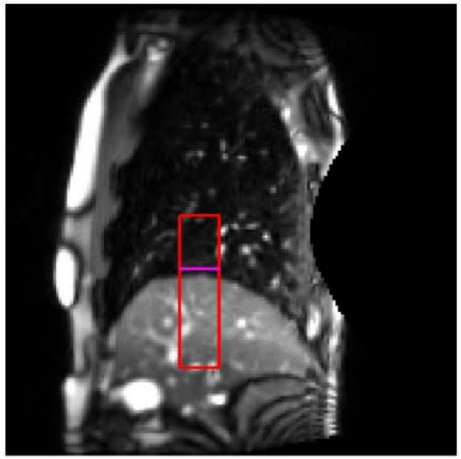
JHU Method 1: PMU QA

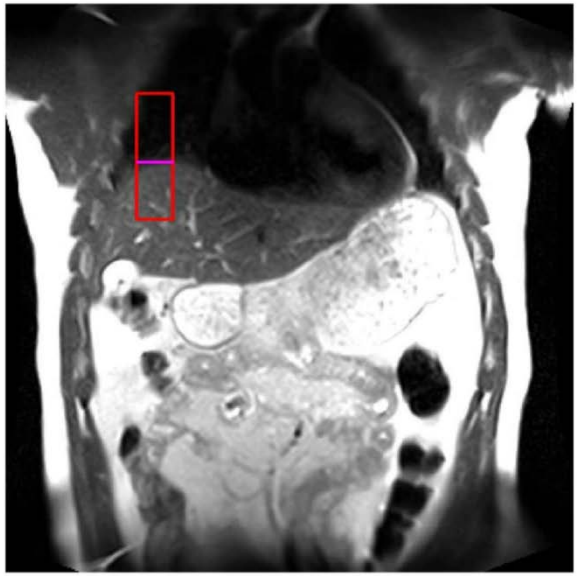
Frequently, the first-pass reconstructions are "garbage."

→ Hypothesis to test was that the PMU clock synchronization is not reliable.

Derive respiratory trace from the diaphragmatic interface:

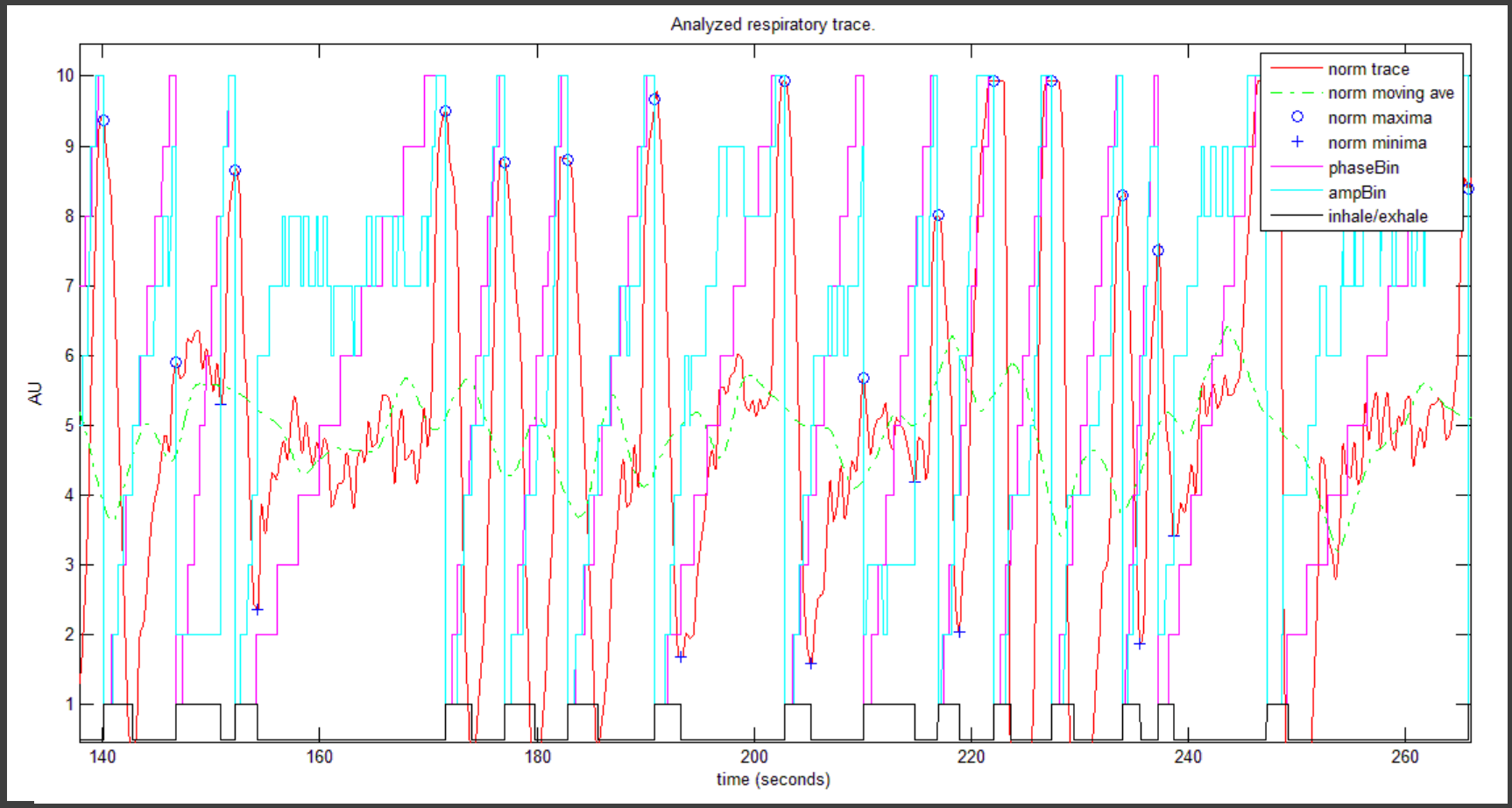
- Challenge: multi-slice study – diaphragm not consistent slice-to-slice
- Define rectangular ROI used in common over all slices





JHU Method 1: ex. case where PMU drifts temporally

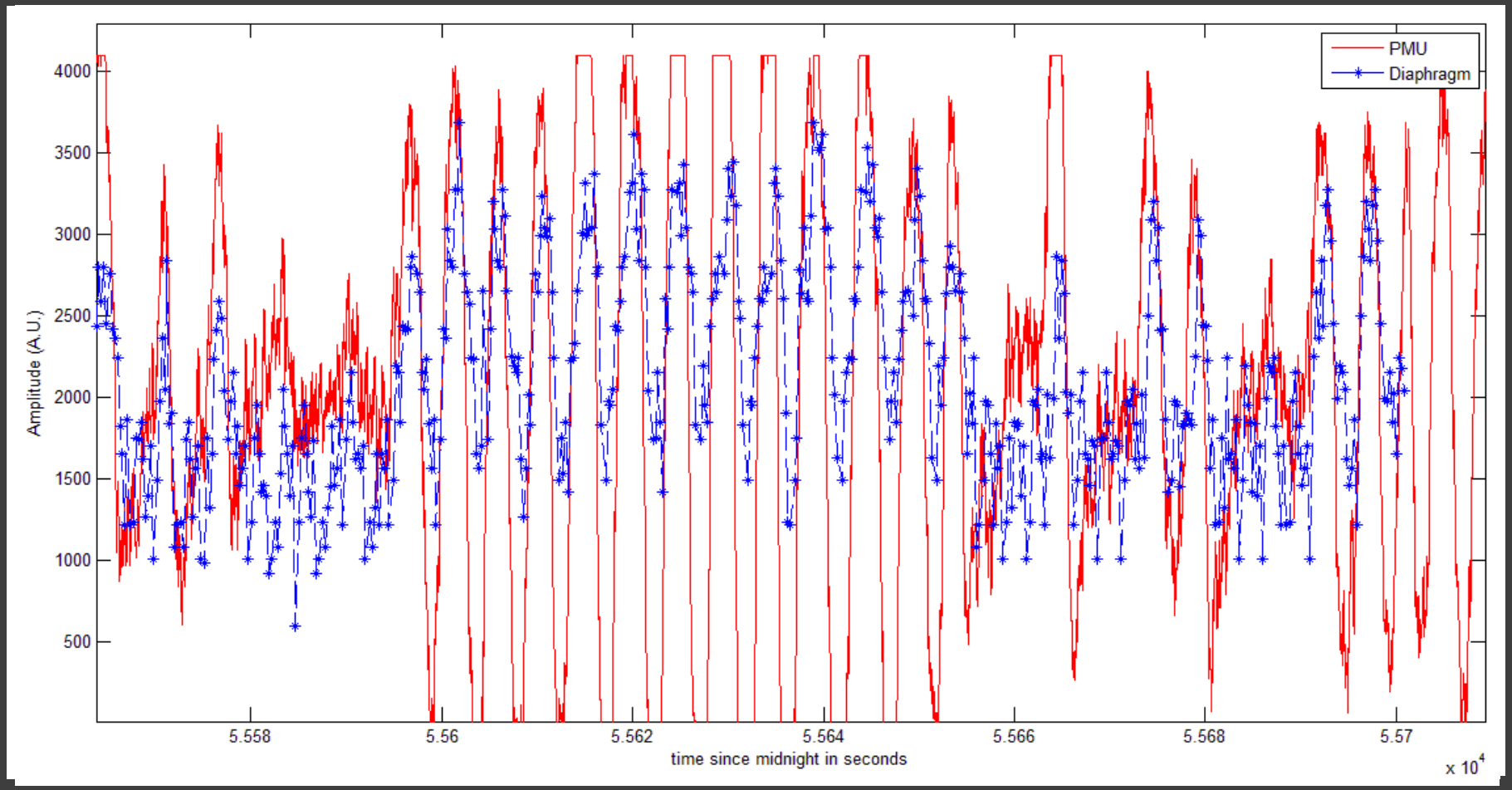
- Sagittal lung bSSFP
- 10 slices for 13 minutes continuously



- Challenging case to start because of breathing pattern
- Assignment of maxima was not 100% robust

JHU Method 1: ex. case where PMU drifts temporally

- Raw PMU trace versus Diaphgragm tracking result
  - Stretched linearly by 1.003

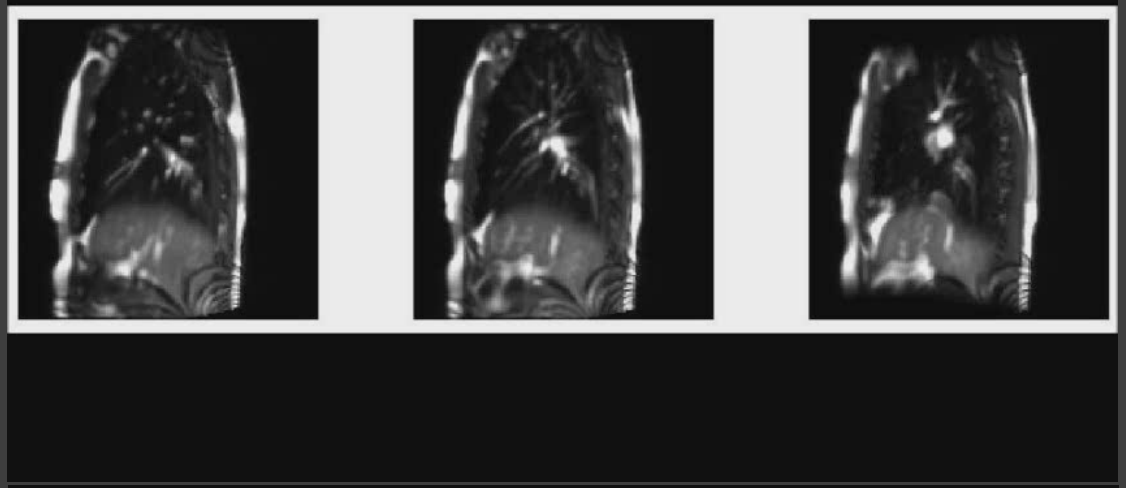


- Out of phase!

JHU Method 1: ex. case where PMU drifts temporally

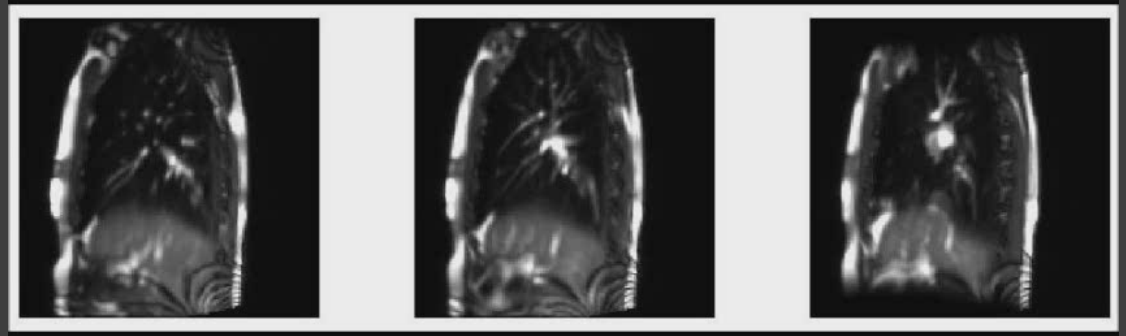
Slice 5/10 Slice 7/10 Slice 9/10

without PMU time scaling:



uncorrelated!

with PMU time scaling (×1.003):

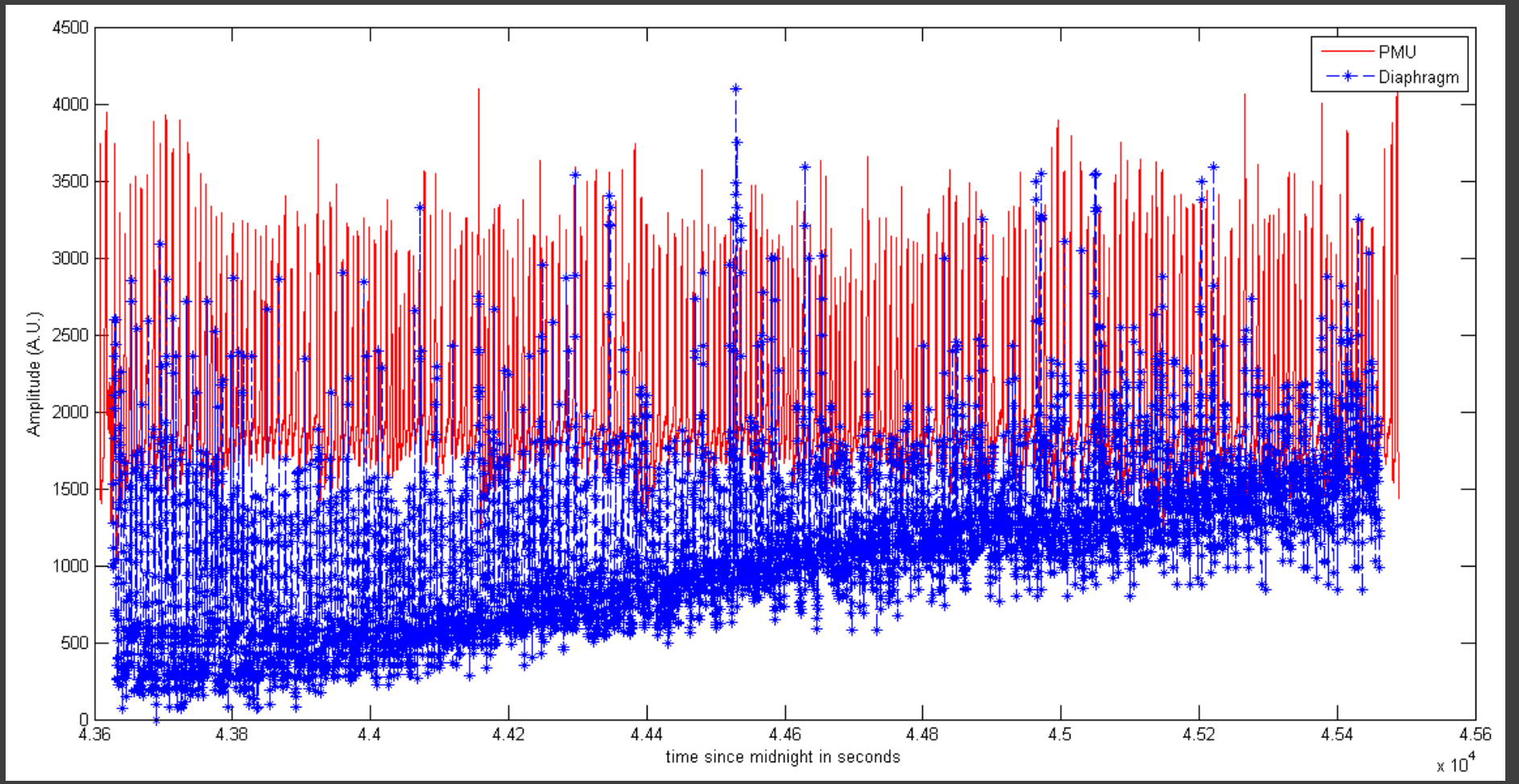


correlated!

JHU Method 1:

diaphragm tracking indicates another challenge:

- Diaphragm position undergoing "baseline drift" over course of 30 minute study



Questions: Should the "representative" 4D-MRI image capture this drift?
If so, how can we do this while preserving image quality?

Conclusions for JHU method 1:

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- We have successfully demonstrated feasibility of this method in volunteers using two readily-available sequences

- Technique will be ready for prime-time when PMU issues are resolved

- Increased frame rates will allow us to scan commensurate anatomical volumes (as 4D-CT) in multiple orientations in a 30 minute MRI session
  (Acquisition speed over 20 frames/sec may be available for bSSFP)

- Although not yet explored, diaphragm signal or other similar image-based surrogates can be used as surrogate for sorting

- Having a long temporal sample capturing all manifestations of variability is good! However, it is unclear, e.g., how best to deal with baseline (diaphragm) shift that may occur

JHU method 2:

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Goal:

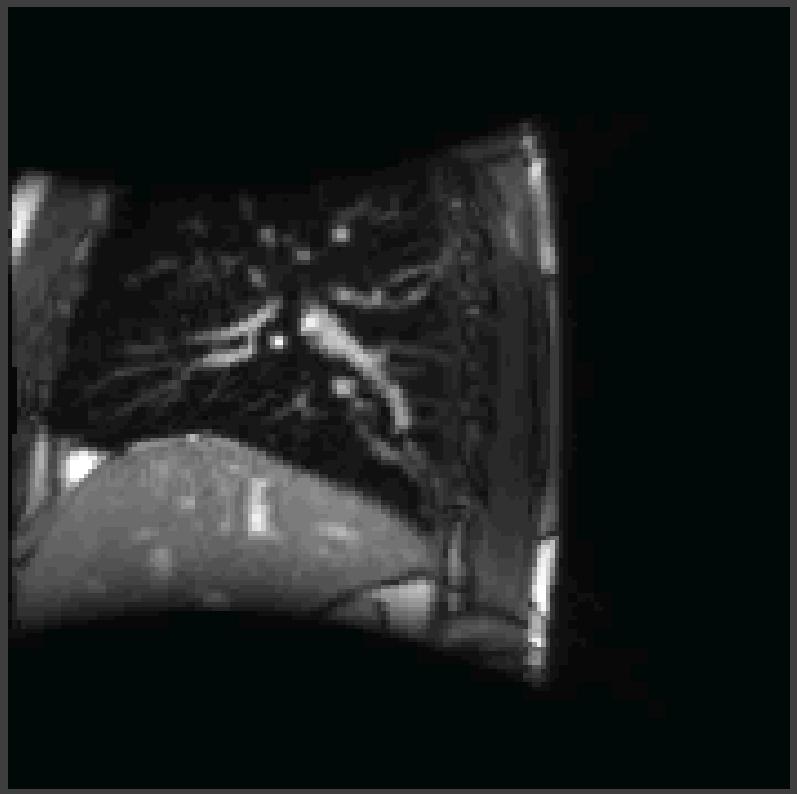
Pre-treatment, perform "true" 4D tracking of the tumor (center of mass) using dMRI over a sufficiently long duration to adequately characterize motion (variability)

Example Applications (not exhaustive list!):

- **Derive the "dynamic internal margin" Coolens et al. [PMB 53(16) 2008]**
- **Derive the spatial-3D probability density function for tumor motion**
- **Allow careful study of spatial-temporal correlations with traditional tumor motion surrogates such as an external respiratory trace or skin/surface markers**
- **Provide the necessary information to determine which potential breathing management strategy is best suited for the given patient, e.g., motion encompassing (ITV), probabalistic, gating, breath holding or tracking**

JHU Method 2: image acquisition

Acquire orthogonal 2D (Sagittal + Coronal) dMRI Siemens MAGNETOM Espree 1.5T

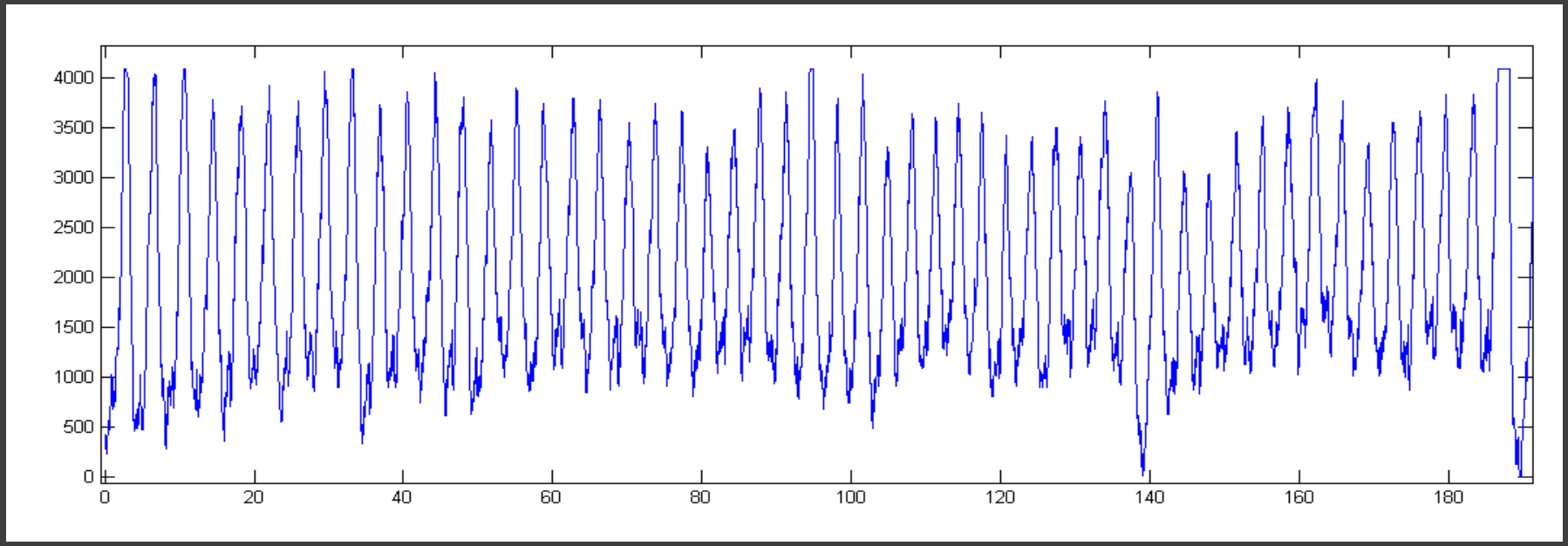


TrueFISP (bSSFP):

- interleaved acquisition (sag, coronal, sag…)
- 2x2 mm^2 pixels in plane
- slice thickness adjusted for motion out-of-plane
- Acquisition speed: ≈4 frames/sec.

JHU method 2: simultaneous respiratory monitoring

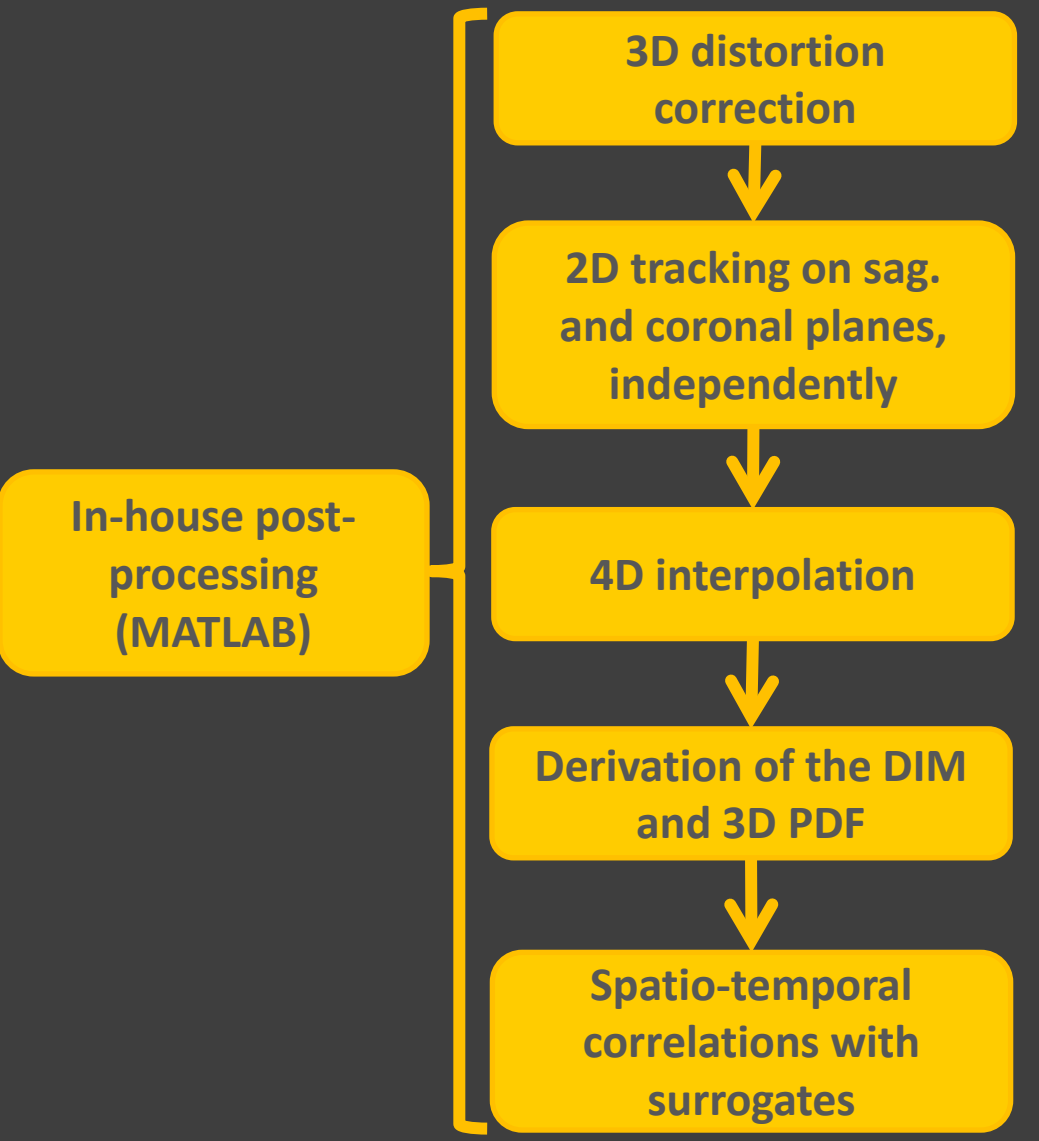
Acquire external respiratory signal (Physiological Monitoring Unit -- PMU)



PMU logging:

- synchronized with the image acquisition computer
- auto started/stopped within sequence run
- sampled at 50 Hz

Methods: post processing



4D interpolation:

- Based on ROIs, template images chosen from an arbitrary frame

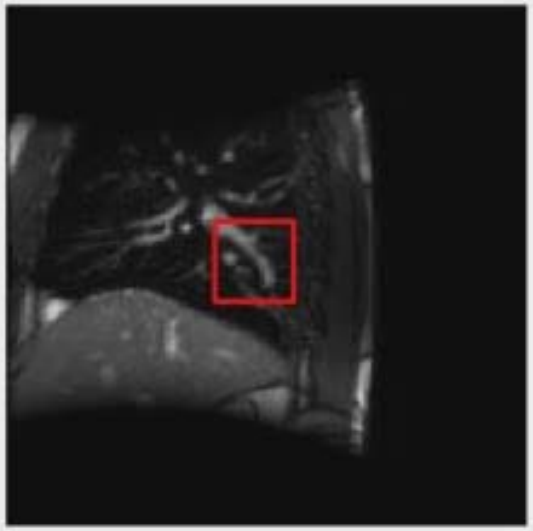
Work in progess!

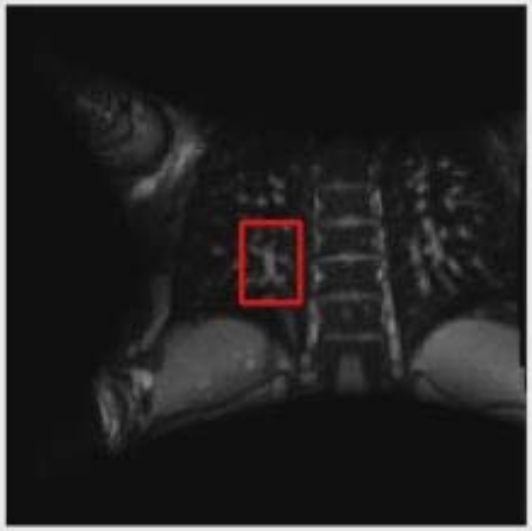
- 2D normalized cross-correlation-based tracking/optimization

Work in progess!

- Images up-sampled 4× to provide higher (spatial) tracking resolution

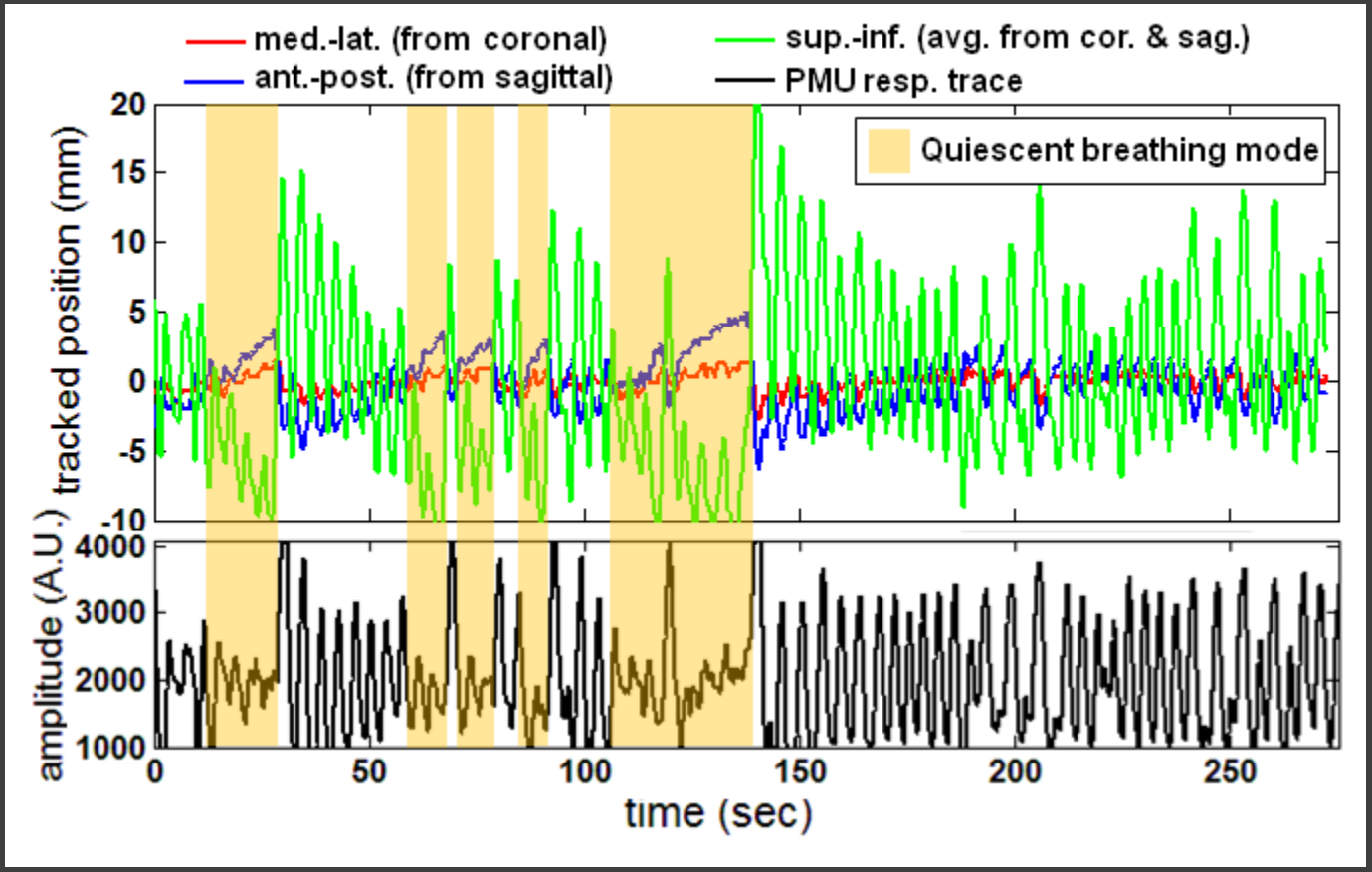
JHU method 2:
Example lung volunteer tracking result





JHU method 2:
Example lung volunteer tracking result, cont'd.

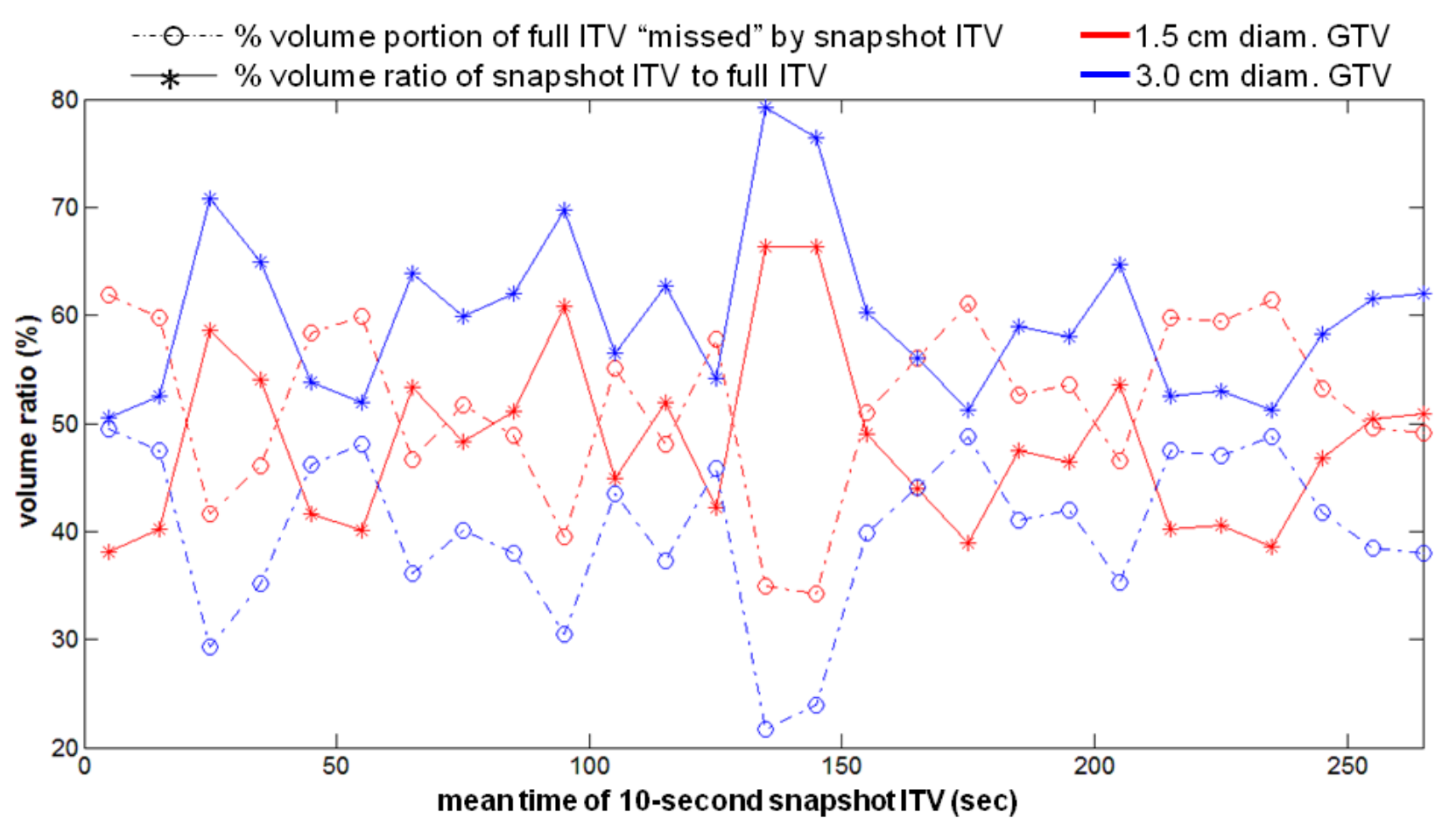
- Volunteer instructed to relax and breathe normally – breathing motion is highly variable
- Two discernable breathing modes detected
- In the "quiescent" state, the PMU correspondence is essentially lost



JHU method 2:

Example lung volunteer tracking result, cont'd.

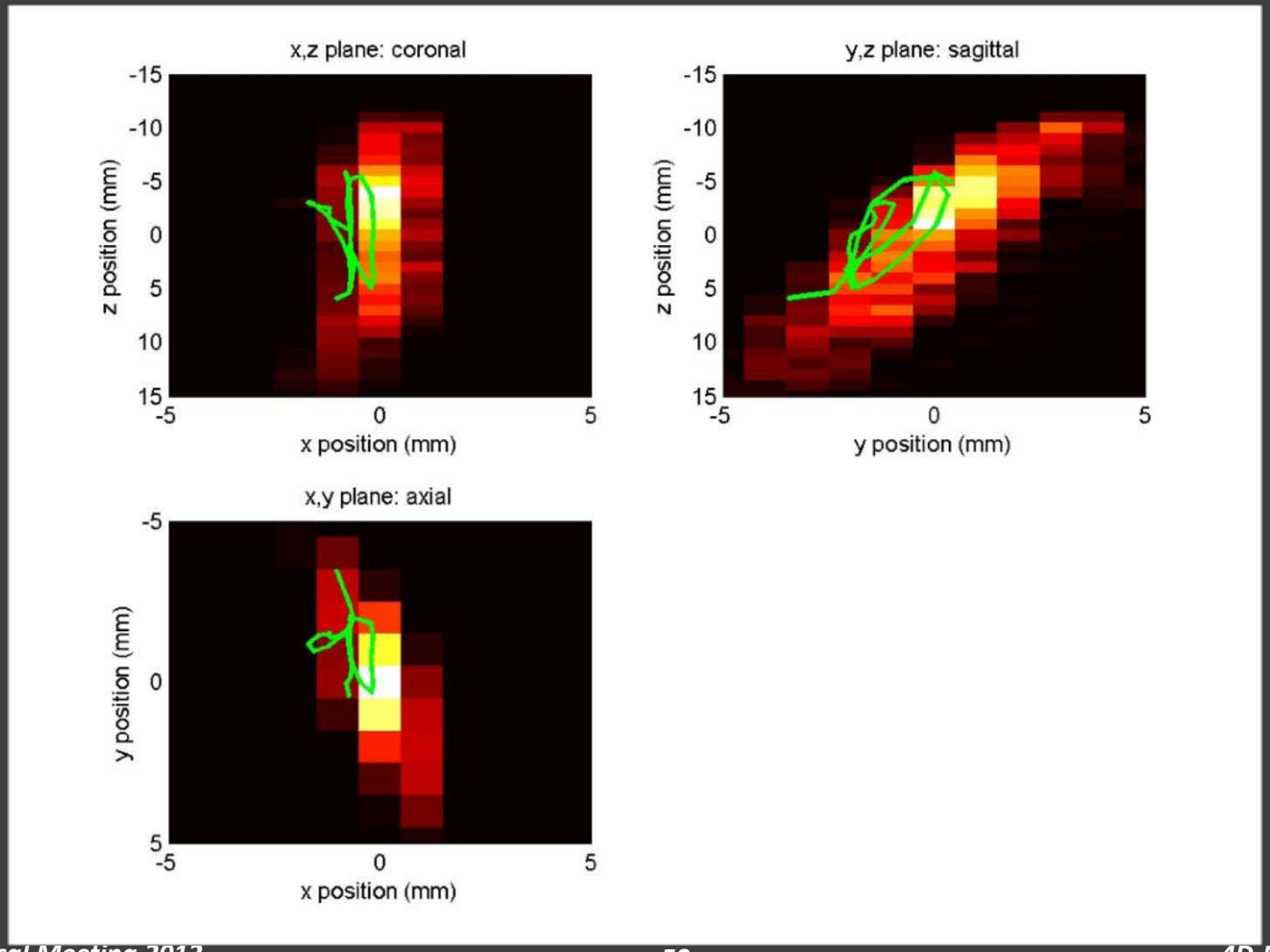
- A typical 4D-CT scan may scan through the tumor in ~10 seconds
- Suppose we compare the full motion ITV vs. 10-second snapshot ITVs for a 1.5 and 3.0 cm (diameter) hypothetical GTV



JHU method 2:

Example lung volunteer tracking result, cont'd.

- A typical 4D-CT scan may scan through the tumor in ~10 seconds
- Suppose we compare the full motion PDF vs. 10-second motion trajectories:

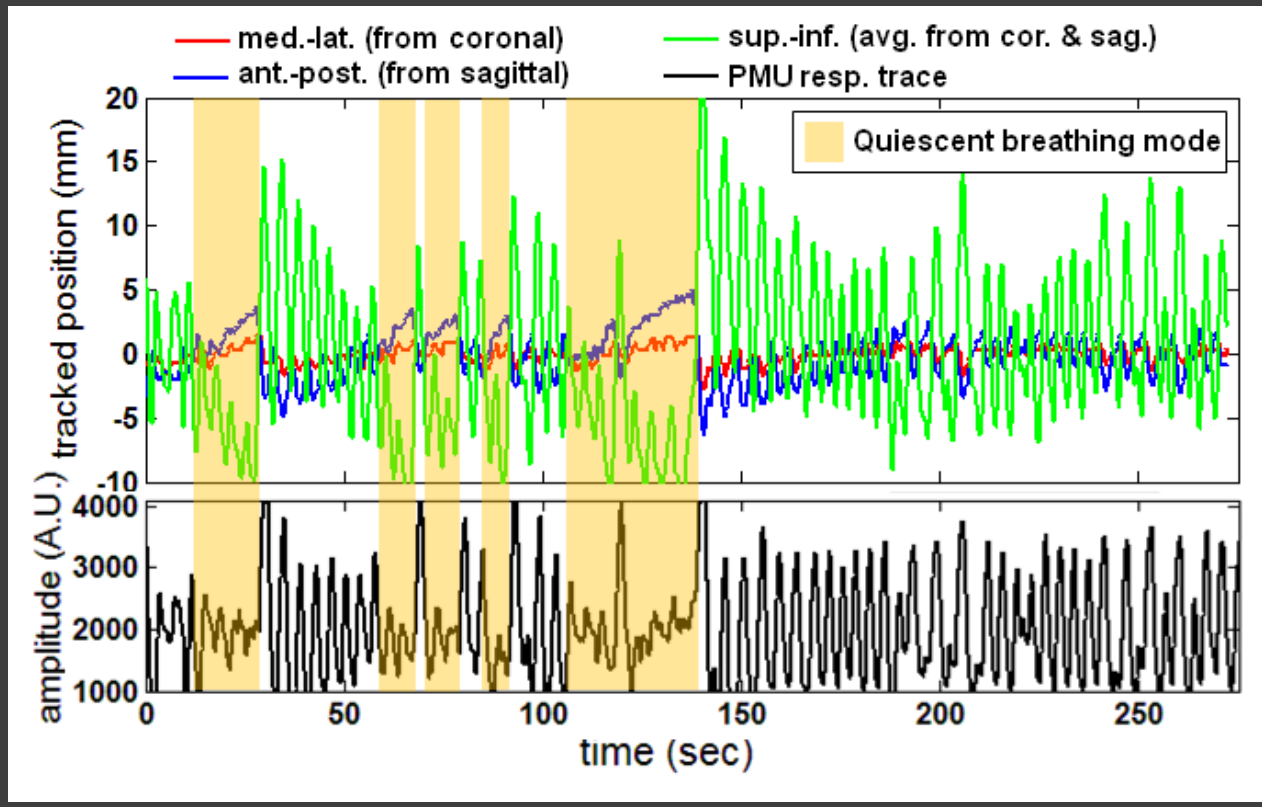


JHU method 2:
Example lung volunteer tracking result, cont'd.

- **Numerical 4D dose accumulation simulations**

Suppose we "scan through" the tumor at times t=130-140 sec. and generate an ITV plan:

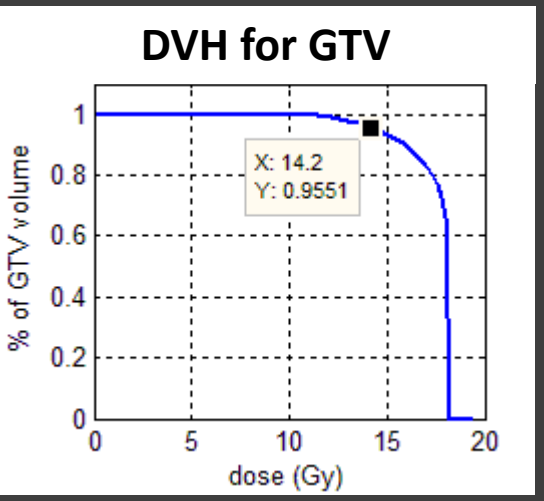
- GTV diameter = 1.5 cm
- PTV = ITV + 1 mm uniform expansion
- $D_{Rx,\ PTV}$ = 18 Gy
- Quasi-realistic dose cloud: uniform in PTV; dose fall-off given by Gaussian tail with 3.5 mm sigma
- Assume "shift invariance"



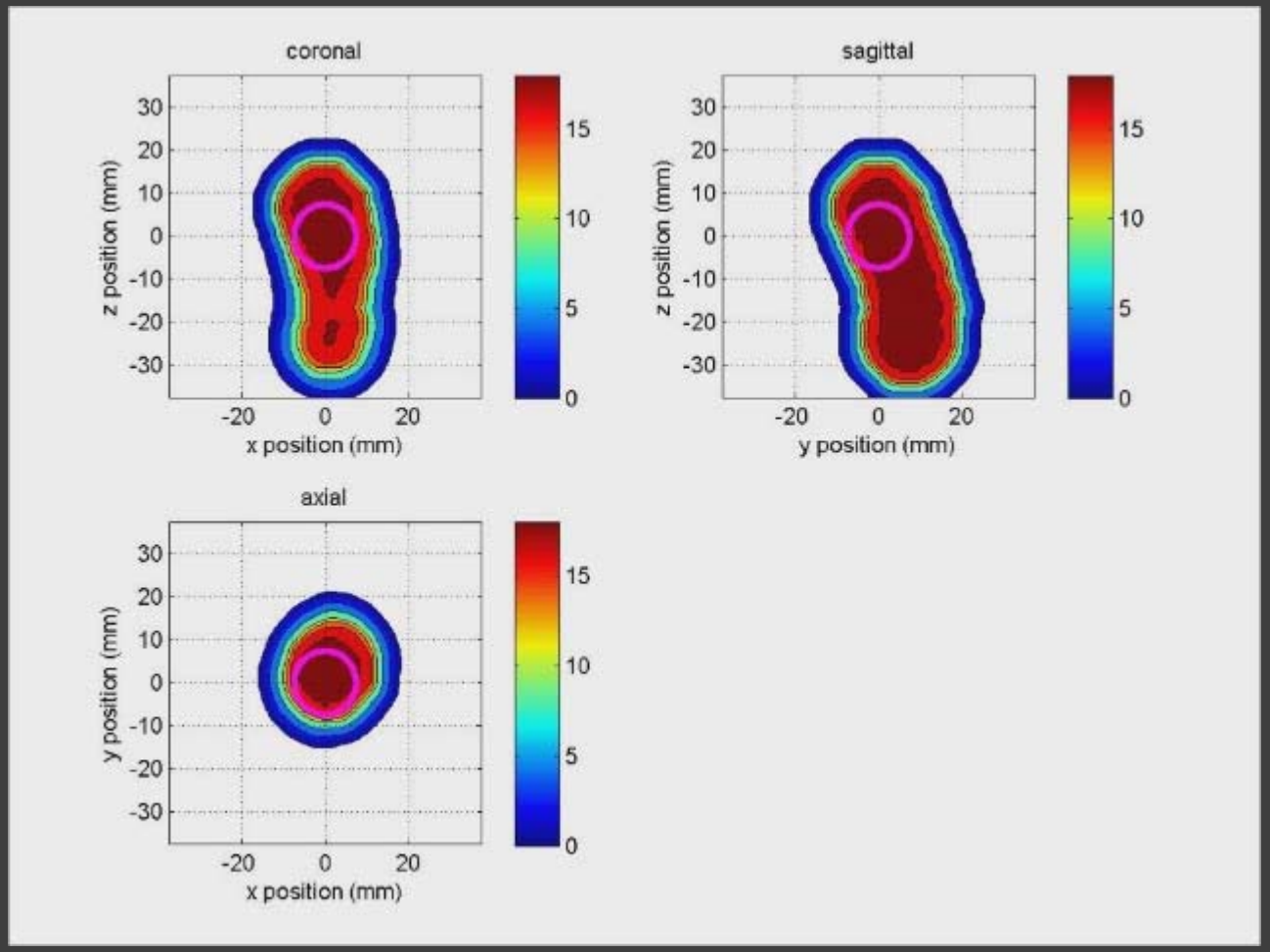
JHU method 2:
Example lung volunteer tracking result, cont'd.

- Numerical 4D dose accumulation simulations to illustrate utility

Suppose we now treat the patient over time, t=30-60 sec:

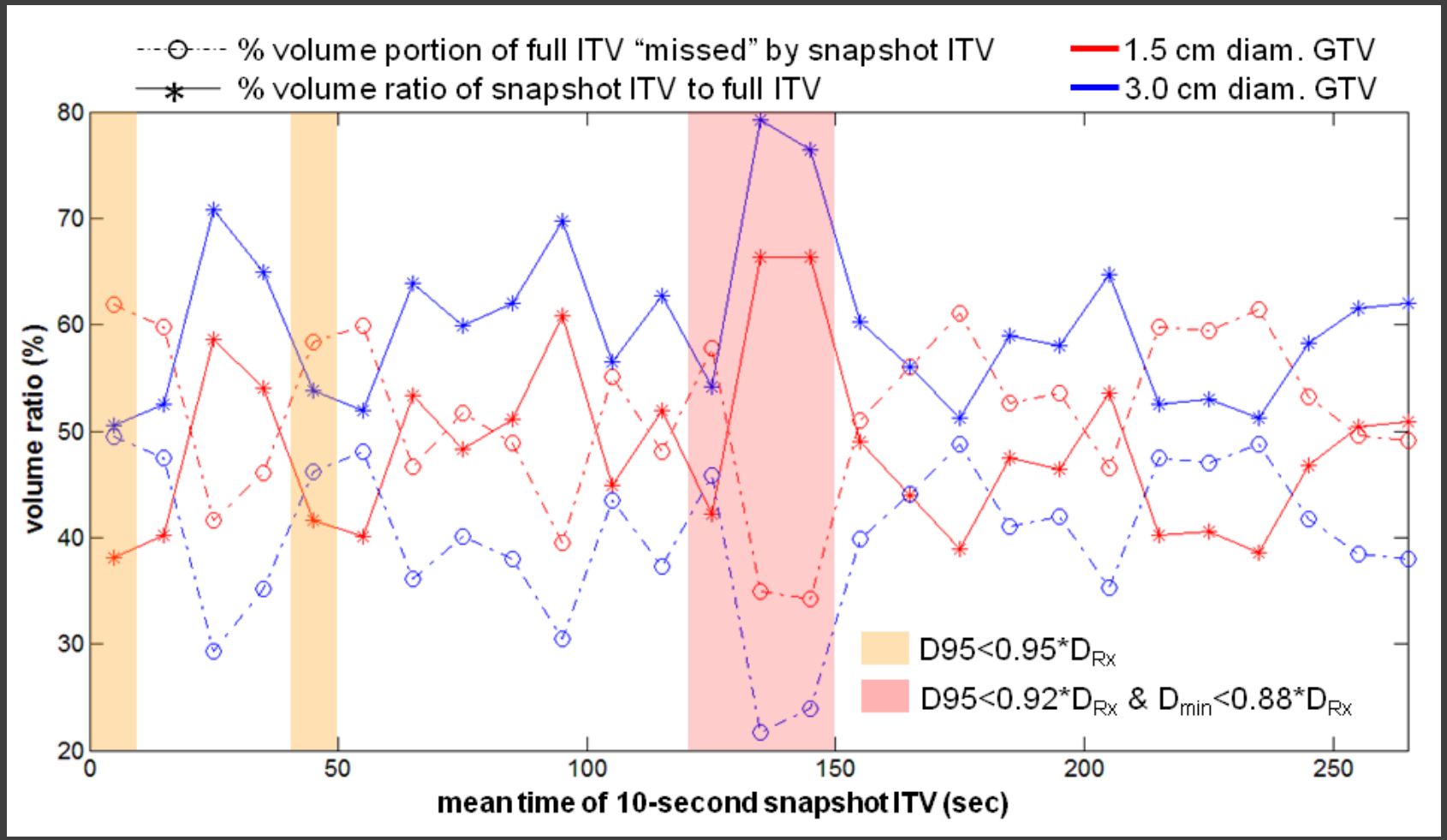


- $D_{min,GTV}$ = 10.4 Gy
- D95 = 14.3 Gy



JHU method 2:
Example lung volunteer tracking result, cont'd.

- Suppose we now move our 10-second snapshot ITV target definition time window iteratively across the entire tracking duration
- For each iteration perform a 4D dose accumulation for the dose cloud derived from the trial ITV (1.5 cm GTV) using the motion information from the entire duration



Conclusions for JHU method 2:

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- We have successfully demonstrated feasibility of this method in volunteers.

- Current focus is on finding practical ways to incorporate this information into clinical workflow.

- Truly 3D dMRI is highly desirable since additional information is available: e.g., tumor deformation can also be tracked and characterized; more complete study of potential internal/external surrogates can be performed. Tradeoffs between image quality and speed currently challenge this approach.

- There are likely ways to combine the method 2 with method 1 to derive a virtual representation of fully 4D tracking

V. Concluding remarks:

JOHNS HOPKINS MEDICINE

- **Dynamic MRI has matured and is ripe for more widespread application in radiotherapy**

- **More investigation is needed to dosimetrically (and perhaps clinically) demonstrate that "4D-MRI" provides advantages over our present 4D imaging (4D-CT) so as to justify the required investments**

  → At Hopkins we soon hope to begin regularly scanning lung and abdominal patients with repeat 4D-MRI to estimate how robust the clinical 4D-CT-based plans are (dosimetrically speaking)

  → Phantom studies planned also to evaluate the geometrical robustness of the dMRI sequences