Development of 4D-MRI for Radiation Therapy

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2

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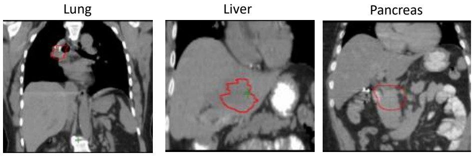
I do not have financial interest with vendors mentioned in this talk.

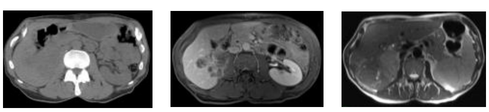
3

Background: CT / 4D-CT



- Accuracy of radiation therapy treatment is challenged by respiration-induced tumor and organ motion.
- 4D-CT has shown great potential in lung cancer treatment, but only has limited use in abdominal motion assessment.

Background: MRI with improved soft tissue contrast



- MRI is well known for its ability to display soft tissue contrast as opposed to X-ray imaging
- X-rays can only discriminate tissues by electron densities, which are not that different between tumor and surround soft tissue.
- In MRI, tissue-specific parameters affect the MR signal (T1, T2, proton density).
- The effect of soft tissue contrast in a MR image of the tissue-specific parameters can be suppressed or enhanced by other parameters (such as TR, TE and flip angle).

Background: Imaging dose

Thoracic 4DCT

Organ	Dose (cGy)
Lung	5.7
Thyroids	7.7
Breasts	4.8
Colon	1.1

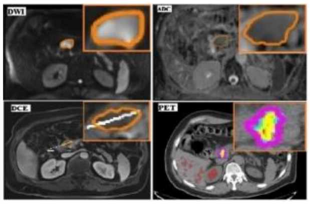
Abdominal 4DCT

Organ	Dose (cGy)
Lung	1.4
Thyroids	0.1
Breasts	1.0
Colon	5.8

J Radiat Res. 2013 Sep; 54(5): 962–970

Associated radiation dose prevents 4DCT to be frequently used in the clinic for motion or treatment response assessments.

Background: MRI with tumor biological information



Dalah E, Moraru I, Paulson E, Erickson B, Li XA et al. Int J Radiat Oncol Biol Phys 2014 Jul 1;89(3):633-40.

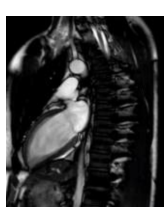
- Both morphological and functional information can be extracted from MR imaging.
- Versatile sequence designs allow for quantitative MR imaging biomarker to be explored.

We need to explore 4D-MRI to guide radiation therapy planning and delivery.

Background: Dynamic MRI

Dynamic MRI (or real-time 4D-MRI or time-resolved 4D-MRI):

- Fast 3D MR sequences
- Fast gradient, parallel imaging, multi-coils
- Compromised SNR and spatial resolution (>3mm)
- Post-imaging processing to improve SNR



MR in RT: MR Pulse Sequences and Image Acquisition (Including Radiation Therapy Applications)
N Yanasak[1]*, K Sheng[2]*, H Gach[3]*
1:45 PM : *Overview of MRI pulse sequences and image acquisition* - N Yanasak, Presenting Author
2:25 PM : *Dynamic MRI for radiation therapy* - K Sheng, Presenting Author
3:05 PM : *Optimizing and troubleshooting MRI for radiation therapy* - H Gach, Presenting Author
MO-DE-702-0 (Monday, July 31, 2017) 1:45 PM - 3:45 PM Room: 702

Background: 4D-MRI based on retrospective sorting/binning

Current CT based radiation therapy planning:
- Planning CT spatial resolution (~1.2 mm in-plane, ~2.5 mm cross-plane)
- For SRS or SBRT cases with small tumor targets, 1-2 mm isotropic

Background: 4D-MRI based on retrospective sorting/binning

Current CT based radiation therapy planning:
- Planning CT spatial resolution (~1.2 mm in-plane, ~2.5 mm cross-plane)
- For SRS or SBRT cases with small tumor targets, ~1 mm isotropic

To generate 4D-MRI dataset amenable to accurate radiation therapy planning:

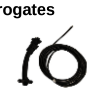
4D-MRI from retrospective binning:
- Fast 2D/3D MR sequences, repetitive scans
- Respiratory surrogates for resorting the data in the imaging domain or from k space
- Adequate image quality, high spatial resolution (<2 mm in-plane, 1-5 mm cross-plane)
- Unable to reflect inter-cycle variations in the respiration pattern

Background: Respiratory surrogates

Internal surrogates
- Diaphragm motion
- Body area
- Deformable image registration
- Fourier transform of the k space line

External surrogates

Bellow system from GE (stretch device)



PMU system from Siemens (pressure belt)

Background: 4D-MRI categorized by sampling trajectories

1. 4D-MRI from resorting images acquired using 2D sampling strategies/sequences; Respiratory phase/amplitude binning happens in the imaging domain after the image reconstruction.

Background: 4D-MRI categorized by sampling trajectories

1. 4D-MRI from resorting images acquired using 2D sampling strategies/sequences; Respiratory phase/amplitude binning happens in the imaging domain after the image reconstruction.

2. 4D-MRI from resorting k space data acquired using 3D MR sampling strategies/sequences; Respiratory binning happens in the k space before the image reconstruction.

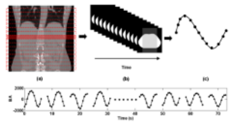
Background: 4D-MRI categorized by sampling trajectories

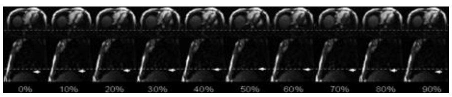
1. 4D-MRI from resorting images acquired using 2D sampling strategies/sequences; Respiratory phase/amplitude binning happens in the imaging domain after the image reconstruction.

4D-MRI strategies similar to 4D-CT.

4D-MRI: Example of internal surrogate (body area, phase sorted)

- T2*/T1 TrueFISP/FIESTA on Siemens 1.5T
- Body area as breathing surrogate
- 1.4x1.4x5 mm^3

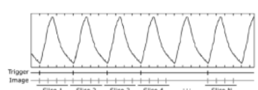


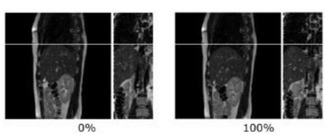


Jing Cai et. al. Med Phys. 2011 Dec; 38(12): 6384-97

4D-MRI: Example of external surrogate (prospective amplitude gated acquisition)

- TSE (turbo spin echo, T2) on a Philips 1.5T
- Bellow pressure system to trigger acquisition
- 2-stage process (preparation and acquisition)
- 1.5x1.5x5 mm^3



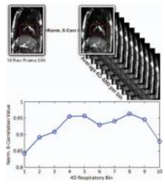


Yanle Hu et.al. Int J Radiat Oncol Biol Phys. 2013 May 1; 86(1): 198–204.

"Snap-shot" 4D-MRI might not reflect the average breathing pattern of an irregular breather.

4D-MRI: Example of external/internal surrogate (w most probable state)

- Intend to solve the problem of "snap-shot" 4D-MRI
- TrueFISP and HASTE on Siemens 1.5T
- PMU, pneumatic device + diaphragm detection
- Phase and amplitude probability-based
- 2-pass sorting (1st pass for average 4D-MRI and 2nd pass for deblurred 4D-MRI using a normalized cross-correlation similarity metric)
- 2x2x5 mm^3



Erik Tryggestad, et. al. Med Phys. 2013 May;40(5):051909.

19

4D-MRI based on 2D acquisition/sampling strategies: Stitching artifacts

J Yang et al. IJROBP V88, No.4, pp. 907-912, 2014

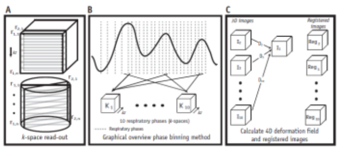
20

2. 4D-MRI from resorting k space data acquired using 3D sampling strategies (sequences); Respiratory binning happens in the k space before the image reconstruction.

21

4D-MRI: k spaced sorted

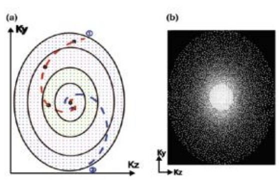
- bTFE (3D balanced turbo field echo) on Philips 1.5T
- Cartesian or radial in-plane sampling
- Navigator placed on the diaphragm or bellow system
- k space sorting
- 2x2x4 mm^3



Bjorn Stemkens, et. al. Int J Radiat Oncol Biol Phys. 2015 Mar 1;91(3):571-8

4D-MRI: k spaced sorted (ROCK)

- bSSFP (balanced steady-state free-precession) on Siemens 1.5T
- Novel rotating Cartesian k-space (ROCK) sampling
- Self gated centerline
- 1.2x1.2x1.6 mm^3



Han F, Zhou Z, Cao M, Yang Y, Sheng K, Hu P. Med Phys. 2017 Apr;44(4):1359-1368.

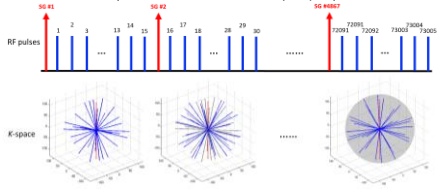
4D-MRI: Cedars approach

Respiratory phase/amplitude resolved 4D-MRI

1) 3D radial acquisition
   - 1.6mm isotropic high resolution.
2) Fixed scan time of ~6 minutes
   - Obtaining averaged breathing pattern
3) Self-gating (SG)
   - Direct monitoring of respiratory motion.
4) Retrospective binning of *k*-space raw data
   - Further enable averaged breathing pattern

4D-MRI: Cedars approach

Spoiled Gradient recalled Echo (GRE) sequence



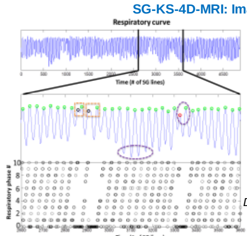
a. RF pulses:
   Self-gating (SG) k-space lines collected in the superior-inferior (SI) direction at every 15 radial projection intervals
   Temporal interval of ~98ms between each SG line

b. K-space:
   3D *k*-space trajectory via radial 2D golden means ordering

25

4D-MRI: Cedars approach

SG-KS-4D-MRI: Image Reconstruction

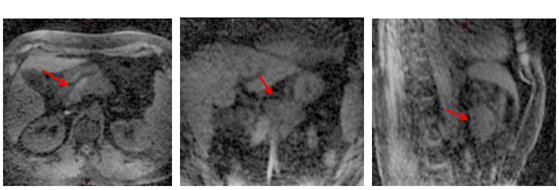


- Respiratory curve was extracted from the time-series SG lines.
- Analyze curve to discard outliers.
- Valid projections were rebinned to 10 phases.
- Reconstruct 4D-MRI using SENSE method.

Deng Z et. al Magn Reson Med. 2015. PMID: 25981762

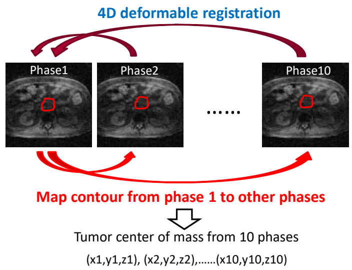
26

SG-KS-4D-MRI; Cedars approach



27

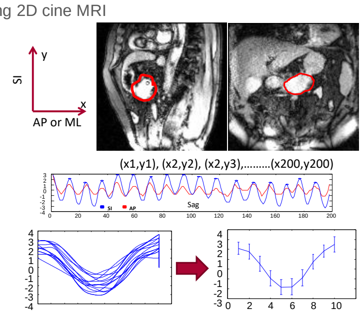
Tumor motion trajectory analysis: 4D imaging (MR or CT)



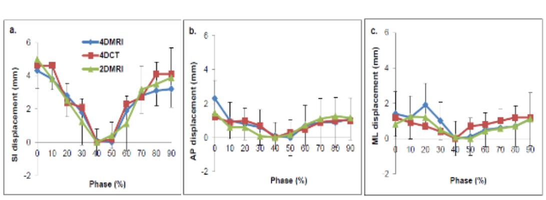
4D-MRI: Validation using 2D cine MRI

Cine 2D-MRI

- Template matching was used to extract tumor motion trajectory from the time-series cine 2D-MRI
- SI and AP motion was extracted from sagittal images
- ML motion was extracted from coronal images

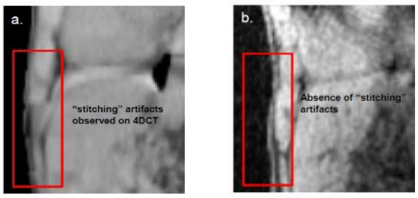


4D-MRI: Evaluation of tumor motion trajectories



4D-MRI: Comparison to 4D-CT

4DCT **SG-KS-4D-MRI**



4D-MRI: Evaluation of tumor motion trajectories for pancreatic cancer patients

Patient	D_{diff} (mm) SG-KS-4D-MRI vs. 4DCT			SG-KS-4D-MRI vs. 2DMRI		
	SI	AP	ML	SI	AP	ML
1a	0.45	0.23	0.42	0.43	0.29	0.21
1b	1.28	0.55	0.42	0.38	0.45	0.40
2	0.57	0.51	0.26	0.32	0.53	0.43
3	N/A	N/A	N/A	0.70	0.45	0.61
4	1.15	0.43	0.47	1.16	0.83	1.02
5	1.71	0.93	0.6	1.93	0.34	0.60
6	1.72	0.70	1.14	1.07	0.44	0.38
7	1.32	0.29	0.26	0.35	0.23	0.75
8	0.81	0.85	0.42	1.43	0.24	0.25
9	1.02	0.46	0.44	0.71	0.32	0.39
10	0.88	0.31	0.31	0.62	0.32	0.28
Mean	1.09	0.53	0.47	0.83	0.40	0.48
σ	0.43	0.24	0.26	0.52	0.17	0.24

- D_{diff}: The difference of the tumor displacements between two imaging modalities calculated for each phase
- Small (<2mm) D_{diff} was observed comparing SG-KS-4D-MRI to 4D-CT/cine 2D-MRI.

4D-MRI: Evaluation of tumor motion trajectories pancreatic cancer patients

Patient	CC SG-KS-4D-MRI vs. 4D-CT			SG-KS-4D-MRI vs. 2D-MRI		
	SI	AP	ML	SI	AP	ML
1a	0.97	0.82	0.41	0.96	0.81	0.88
1b	0.97	0.72	0.28	0.97	0.89	0.59
2	0.94	0.66	0.89	0.96	0.60	0.84
3	N/A	N/A	N/A	0.94	0.85	0.91
4	0.92	0.47	0.45	0.91	0.81	0.32
5	0.92	0.92	0.58	0.92	0.92	0.7
6	0.83	0.45	0.16	0.86	0.70	0.94
7	0.83	0.86	0.04	0.90	0.89	0.58
8	0.83	0.87	0.63	0.92	0.82	0.85
9	0.93	0.75	0.45	0.93	0.91	0.75
10	0.92	0.72	0.55	0.94	0.89	0.73
Mean	0.91	0.72	0.44	0.93	0.83	0.74
σ	0.06	0.16	0.24	0.03	0.10	0.18

- CC: Correlation coefficients calculated from tumor trajectories of two imaging modalities.
- Good correlations (CC>0.9) were observed between SG-KS-4D-MRI and 4DCT/cine 2D-MRI in SI direction.
- Correlations between SG-KS-4D-MRI and 4DCT/cine 2D-MRI in AP and ML directions are not as good as those in SI direction, possibly due to smaller motion magnitudes in these two directions.

4D-MRI: Evaluation of tumor volume for pancreatic cancer patients

GTV_σ (cc)		
Patient	SG-KS-4D-MRI	4DCT
1a	0.66	0.57
1b	0.60	0.63
2	1.71	2.20
3	0.69	N/A
4	0.38	0.71
5	1.73	1.82
6	1.26	1.67
7	0.24	0.47
8	0.09	0.12
9	0.82	1.02
10	0.77	0.98
Mean	0.81	1.02
σ	0.54	0.67
p	0.012*	

- GTV_σ: Standard deviation of GTVs calculated from ten phases for each patient
- SG-KS-4D-MRI shows a consistently smaller GTV_σ comparing to 4D-CT for all patients.
- Wilcoxon rank test between the two groups shows a p value of 0.012, indicating a statistically significant difference.
- Possibly due to the stitching artifacts present in 4D-CT resulting a more variable tumor boundary definition

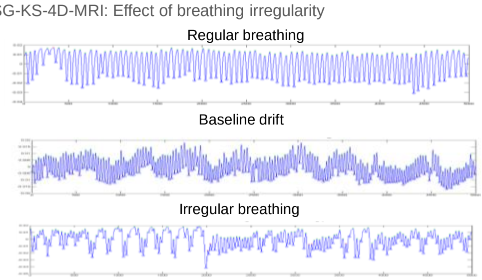
34

Initial experience of SG-KS-4D-MRI on pancreatic cancer patients

- Absence of stitching artifacts
- Average motion trajectory agrees well with 2D cine MRI and 4D-CT in SI direction
- Less variation in tumor volumes across ten respiratory bins comparing to 4D-CT.

35

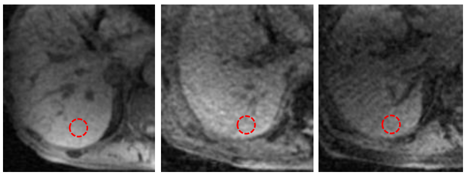
SG-KS-4D-MRI: Effect of breathing irregularity



36

SG-KS-4D-MRI: Effect of breathing irregularity

	Regular breathing	Baseline drift	Irregular breathing



Noise:	**7.2%**	**9.9%**	**10.3%**

Noise: the standard deviation divided by the average voxel intensities within a selected volume.

37

4D-MRI: Improving image quality by non-local means denoising

西安电子科技大学 XIDIAN UNIVERSITY

CEDARS-SINAI. SAMUEL OSCHIN COMPREHENSIVE CANCER INSTITUTE DEPARTMENT OF RADIATION ONCOLOGY

Non-local means denoising : Use the mean values of distant pixels to enhance the signal to noise ratio based on the similarity to the target pixel.

Nonlocal Means Denoising of Self-Gated and k-Space Sorted 4-Dimensional Magnetic Resonance Imaging Using Block-Matching and 3-Dimensional Filtering: Implications for Pancreatic Tumor Registration and Segmentation.
Int J Radiat Oncol Bio Phys 2016 Jul 1;95(3):1058-1066. Jin J. Gou S. Yang W et. al.

38

4D-MRI: Improving image quality by block matching 3D (BM3D)

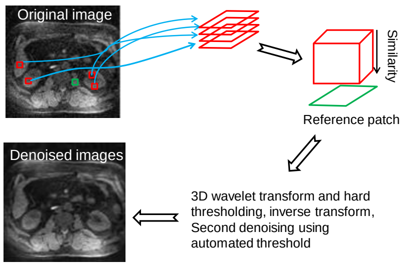
2080 IEEE TRANSACTIONS ON IMAGE PROCESSING, VOL. 16, NO. 8, AUGUST 2007

Image Denoising by Sparse 3-D Transform-Domain Collaborative Filtering

Kostadin Dabov, *Student Member, IEEE*, Alessandro Foi, Vladimir Katkovnik, and Karen Egiazarian, *Senior Member, IEEE*

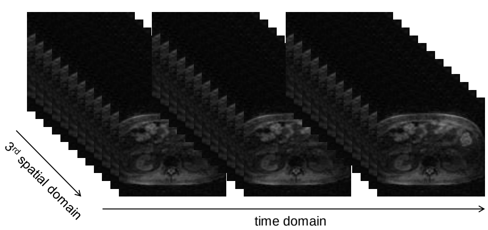
39

4D-MRI: Improving image quality by block matching 3D (BM3D)



40

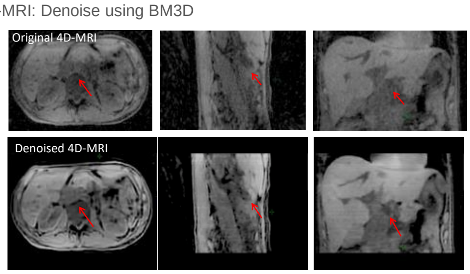
4D-MRI: Extending BM3D in the space and time domains



The additional space and time domain offers more similar patches for block construction

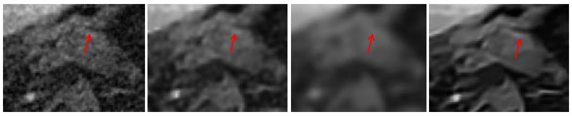
41

4D-MRI: Denoise using BM3D



42

4D-MRI: Comparing BM3D to local denoising method



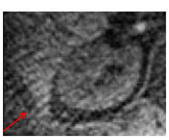
Original | Anisotropic diffusion (low) | Anisotropic diffusion (high) | BM3D

- Anisotropic diffusion using low diffusion coefficient achieves limited denoising effect; to achieve high degree of noise suppression, details are compromised.
- In comparison, BM3D is able to achieve substantial noise suppression while maximally preserving image details.

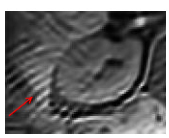
43

4D-MRI: Limitation of BM3D on 4DMRI acquired from 3D sampling

Effective in suppressing random noise but keep artifacts that appear repetitively at the same location



Original



BM3D

Methods such as principle component analysis (PCA) can be used to remove the banding artifacts

44

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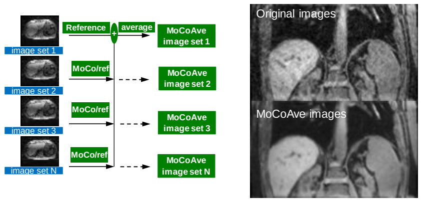
45

4D-MRI: Improving image quality by deformable image registration

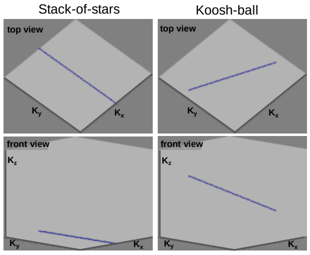
We hypothesize that the quality of 4D images can be improved without compromising motion information by averaging the undersampled bin images after motion correction (MoCoAve).



Slide courtesy of Xiaoming Bi, Jianing Pang, Zhaoyang Fan

46

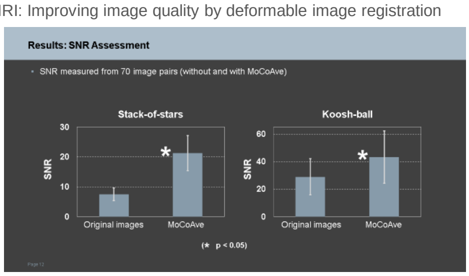
4D-MRI: Two 3D sampling trajectories were tested



Slide courtesy of Xiaoming Bi and Jianing Pang

47

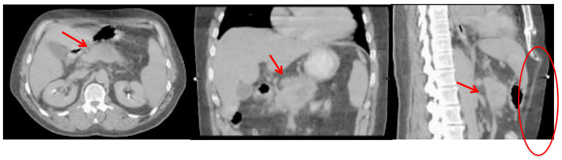
4D-MRI: Improving image quality by deformable image registration



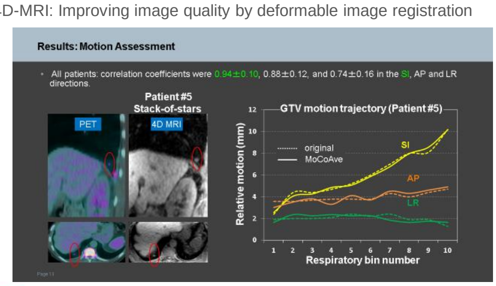
Slide courtesy of Xiaoming Bi, Jianing Pang, Zhaoyang Fan

48

4D-MRI: Comparison to 4D-CT



4D-MRI: Improving image quality by deformable image registration



Slide courtesy of Xiaoming Bi, Jianing Pang, Zhaoyang Fan

Current 4D-MRI techniques:

- Able to provide anatomic motion information.
- Tumor contrast can be enhanced by different MR sequences.
- Imaging quality can be improved by post-imaging processing.

Current 4D-MRI techniques:

- Able to provide anatomic motion information.
- Tumor contrast can be enhanced by different MR sequences.
- Imaging quality can be improved by post-imaging processing.

How do we use it to guide radiation therapy?

1. Incorporating functional MR sequence in 4D-MRI which might give you information differently from anatomy-only imaging.

4D-DWI: a feasibility study; Liu Y, ……, Cai j. Med Phys. 2017 Feb; 44(2):397-406

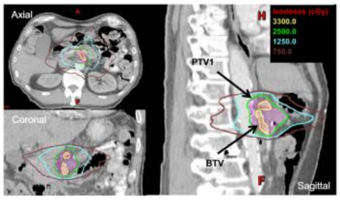
2. Use the motion model extracted from 4D-MRI to create synthetic 4D-CT

A hybrid approach for fusing 4D-MRI temporal information with 3D-CT for the study of lung and lung tumor motion ;Yang YX. et. al. Med Phys. 2015 Aug; 42(8):4484-96

……

4D-MRI: Cedars effort on pancreatic cancer patients

- Pancreatic ductal adenocarcinoma has the worst outcome of any solid tumor.
- Surgical resection remains the most effective therapy to prolong survival.
- Only 15% of patients present with resectable disease, due to primary tumors encompassing and infiltrating vasculatures.
- Overall survival rates in the patients undergoing margin negative resection after neoadjuvant therapy are 2-3 times that of those who remain unresectable.
- Stereotactic body radiation therapy (SBRT) with simultaneous integrated boost (SIB) to tumor infiltrating blood vessels has the potential to sterilize tumor around the vessels and improve resection rates.



Dosimetric evaluation of SIB during SBRT for pancreatic cancer
Yang W, Reznik R, Fraass BA, Nissen N, Hendifar A, Wachsman A, Sandler H, Tuli R. Med Dosim. 2015 Spring;40(1):47-52.

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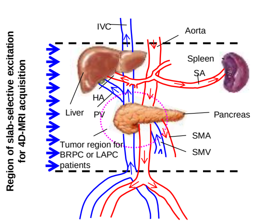
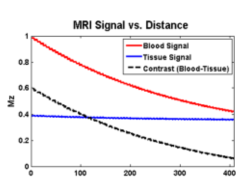
We need to visualize the vessels in the 4D-MRI.

56

4D-MRI: with vessel highlighting

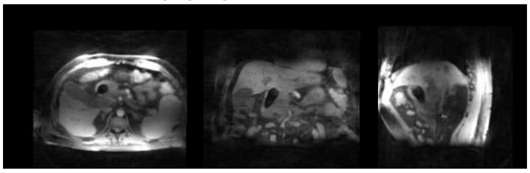




Slab-Selective excitation

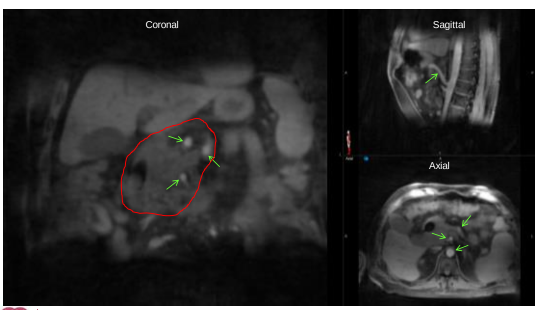
57

4D-MRI: with vessel highlighting



Vessel signals in the 4D-MRI can be enhanced by shrinking the excitation volume.

58



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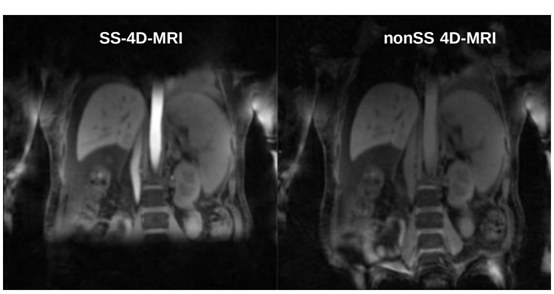

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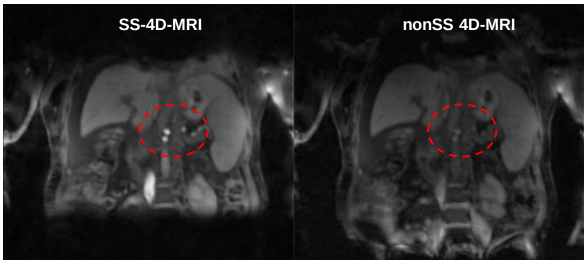


					SS-4D-MRI / 4D-CT		ICC (PTV vs. involved vessels) on SS-4D-MRI		
Patient ID	Gender	Age	GTV (cc)	SI motion (mm)	CNR aorta	CNR IV	SI	AP	ML
1	M	54	220	3.7	13.2 / 0.7	11.2 / 2.9	0.99	0.18	0.97
2	M	79	53	4.2	13.5 / 0.3	4.6 / 0.7	1.00	0.44	0.42
3	M	69	100	3.3	43.8 / 7.3	27.5 / 5.8	0.96	0.88	0.96
4	M	79	38	3.8	14.5 / 1.0	4.7 / 1.6	0.99	0.93	0.87
5	F	48	58	1.5	32.0 / 0.8	23.1 / 0.8	0.81	0.44	0.94
6	M	69	48	2.3	6.2 / 2.0	6.9 / 0.3	0.93	0.72	0.44
7	M	67	87	4.8	14.8 / 1.4	9.1 / 1.4	0.99	0.98	0.63
8	F	79	125	2.3	18.7 / 1.7	11.9 / 6.5	0.69	0.11	1.00
9	M	34	112	7.3	64.2/ 1.9	23.5 / 7.6	1.00	0.92	0.93
10	F	72	14	3.0	9.5 / 3.8	8.7 / 4.4	0.97	0.85	0.52
Average	n/a	65	86	3.6	23.0 / 2.1	13.1 / 3.2	0.93	0.65	0.77
Stdev	n/a	14.3	55.8	1.5	18.3 / 2.0	8.4 / 2.7	0.10	0.31	0.23
p	n/a	n/a	n/a	n/a	**0.002***	**0.001***	n/a	n/a	n/a

GTV=gross tumor volume, SI=superior-inferior, AP=anterior-posterior, ML=medial-lateral, CNR aorta= contrast to noise for aorta, CNR IV= CNR for involved vessel, CC=correlation coefficient

- **Vessel CNR is significantly improved comparing to 4D-CT.**
- **Tumor motion correlates well with vessel motion for most patients.**

Conclusions/Future developments

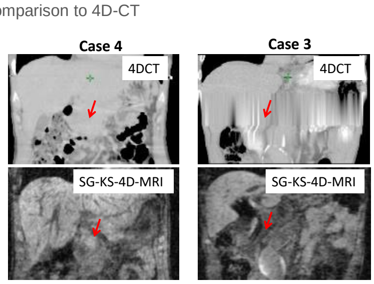
- 4D-MRI with retrospective binning is an active research area now.
- More efforts need to be spent on researching the applications in radiation therapy, standardizing the sequences and workflows.
- Vendor adaptation of the novel 4D-MRI sequences on the scanner is preferred, so more multi-institutional clinical results can be generated.

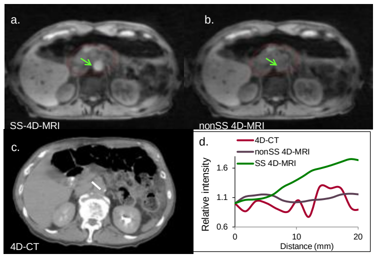
Thank you !

4D-MRI: Validation using 2D cine MRI

Hardware	• 3T MAGNETOM Verio, Siemens • 32 channel surface coil	
Sequence	Real-time 2D MRI	SG-KS-4D-MRI
Imaging Protocol	• 2D Cartesian-sampling • Spoiled GRE sequence • Temporal resolution = 351ms/frame • FOV = 300x300mm² • Spatial resolution = 1.6x1.6mm² • Slice thickness = 8mm • FA = 10º • TR/TE = 4ms/1.64ms • BW = 651Hz/pixel • TA = 1 min	• 3D radial-sampling with golden-angle • Spoiled GRE sequence • SG lines every ~98ms • FOV = 300x300x300mm³ • Isotropic resolution (1.6x1.6x1.6 mm³) • FA = 10º • TR/TE = 5.8/2.6 ms • BW = 399Hz/pixel • TA = 8min

4D-MRI: Comparison to 4D-CT





SS-4D-MRI: Slab-Selective 4 dimensional magnetic resonance imaging; nonSS-4D-MRI: non-Slab-Selective-4D-MRI; 4D-CT: 4 dimensional computed tomography