Advances in Image-guided Neuro-interventions: Clinical Pull and Technology Push in 2D, 3D, and 4D imaging methods

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UW-Madison Stroke Imaging Research Team:

PIs: Guang-Hong Chen, Charlie Strother, and Beverly Aagaard-Kienitz

Members (Basic Science):

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Members (Clinical):

Howard Rowley, Pat Turski, David Niemann, Azam Ahmed

Siemens Support: Sebastian Schafer, Kevin Royalty, Yu Zheng, Klaus Klingenbeck

International Clinical Collaborators: Dr. Pengfei Yang at Chang Hai Hospital, Shanghai, Drs. Doerfler and Struffert at the University of Erlangen-Nuremberg

Outline

- Technical challenges and technical solution, SMART-RECON, to address the challenges
- SMART-3D: generate 3D DSA and soft tissue images with reduced motion artifacts, beam hardening artifacts and noise level from a single sweep cone-beam CT (CBCT) acquisition
- SMART-4D: generate time-resolved CBCT angiography and whole brain CBCT perfusion maps
- SMART-2D in angio suite: factor of 20 reduction of radiation dose in 2D DSA
- Summary

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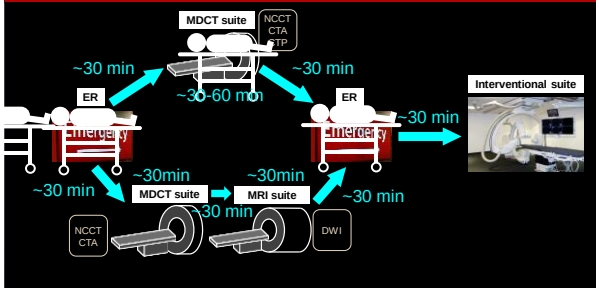
Clinical motivations: Current clinical workflow for acute ischemic stroke patients

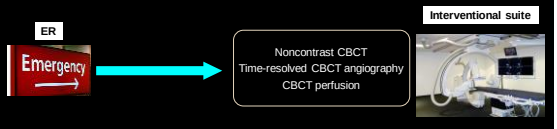


Procedure characteristic in published clinical trials

- Procedure characteristics in EXTEND-IA Trial
  - ONSET TO GROIN PUNCTURE 210 (166-251)
  - **CT TO GROIN PUNCTURE 93 (71-138)**
  - GROIN PUNCTURE TO TICI 2B/3 OR COMPLETION 43 (24-53)
  - ONSET TO TICI 2B/3 OR COMPLETION 248 (204-277)

Much shorter time from imaging to groin puncture is desired for better treatment outcome for eligible subjects!

One-stop-shop imaging workflow in angio-suite

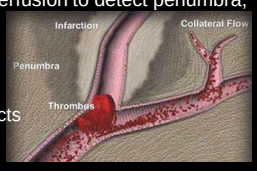


Imaging *needed* in One-Stop-Shop workflow

- Non-contrast whole brain cone beam CT image to detect hemorrhage;
- Time-resolved CBCT angiography to locate occlusion site and collaterals;
- Whole brain cone-beam CT Perfusion to detect penumbra;

Plus:

- Reduced motion artifacts;
- Reduced radiation dose;
- Reduced beam hardening artifacts
- ……



Visualizing hemorrhage in Angio suite: A comparison of cone beam CT and MDCT

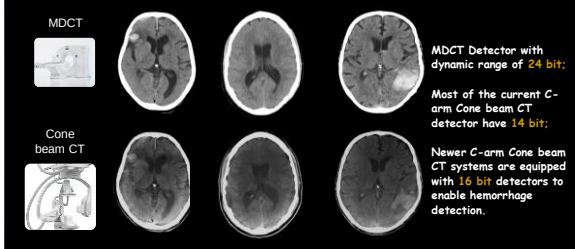


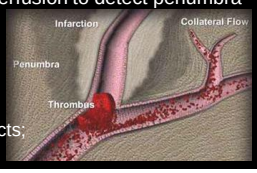
Image courtesy of Prof. Skalej, Neuroradiology, Magdeburg. Image acquired with Siemens Artis Q.

Imaging *needed* in One-Stop-Shop workflow

- Non-contrast whole brain cone beam CT image to detect hemorrhage; ✓
- Time-resolved CBCT angiography to locate occlusion site and perform collateral analysis;
- Whole brain cone-beam CT Perfusion to detect penumbra and infarction core;

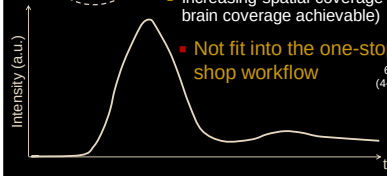
Plus:

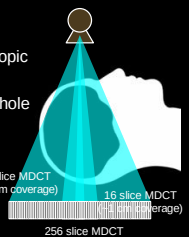
- Reduced motion artifacts;
- Reduced radiation dose;
- Reduced beam hardening artifacts;
- ……



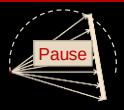
MDCT perfusion imaging: State-of-the-art

- High temporal resolution and temporal sampling density
- Decent spatial resolution (isotropic 0.5mm)
- Increasing spatial coverage (whole brain coverage achievable)
- Not fit into the one-stop-shop workflow

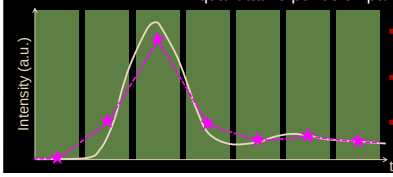




Cone beam CT perfusion: Idea and Challenges

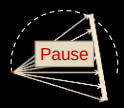


- Low temporal sampling density: from few data points (7-10) to recover contrast uptake curve;
- Low temporal resolution: from temporally averaged inaccurate measurements to obtain quantitative perfusion parameters.



- Whole brain spatial coverage;
- High spatial resolution (better than 0.3mm);
- Nicely fit into one-stop-shop workflow!

Technical challenge: brief summary



Slow C-arm Gantry

High Temporal resolution and high temporal sampling density needed for perfusion imaging

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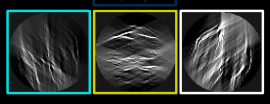
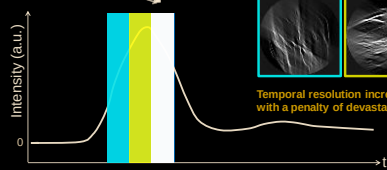
Small angular sector to increase temporal resolution: A very simple idea

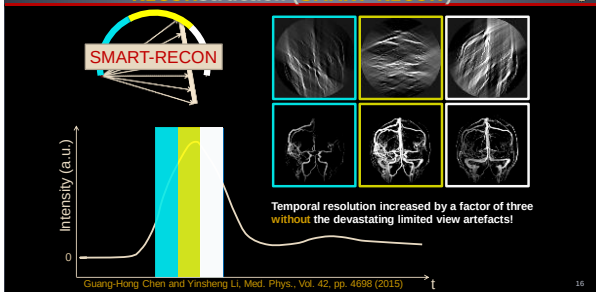
Conventional Filtered Backprojection (FBP) Reconstruction





Temporal resolution increased by a factor of three with a penalty of devastating limited view artefacts!

Synchronized Multi-Artifacts Reduction in Tomographic RECONstruction (SMART-RECON)



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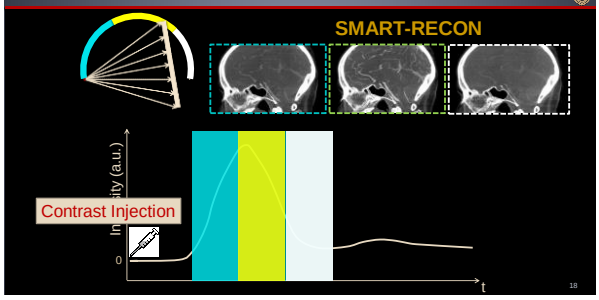
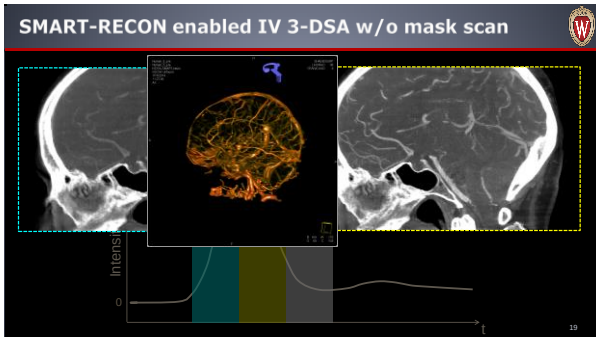
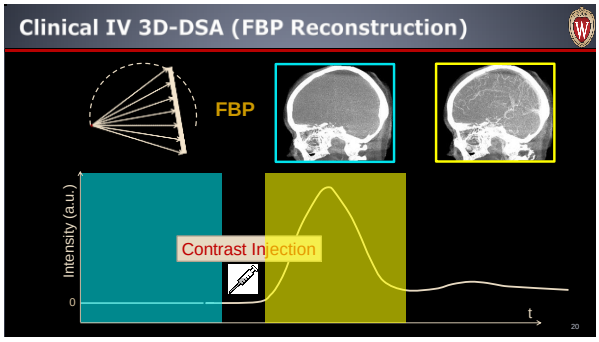
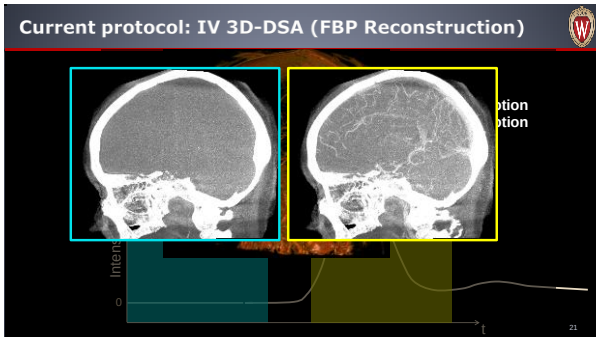
SMART-RECON enabled IV 3D-DSA w/o mask scan

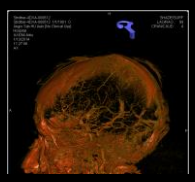


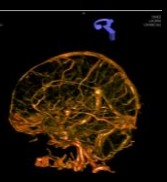

SMART-RECON enabled IV 3-DSA w/o mask scan
Intens
0
t
19


Clinical IV 3D-DSA (FBP Reconstruction)
FBP
Intensity (a.u.)
Contrast Injection
0
t
20


Current protocol: IV 3D-DSA (FBP Reconstruction)
Intens
0
t
21

Clinical IV 3D-DSA vs SMART-RECON IV 3D-DSA





- Inter sweep motion
- Intra sweep motion
- Doubles radiation dose

Clinical IV 3D-DSA

- NO inter sweep motion
- Much reduced intra sweep motion
- Factor of TWO radiation dose reduction!

SMART-RECON IV 3D-DSA

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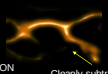
Clinical IV 3D-DSA vs SMART-RECON IV 3D-DSA

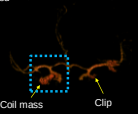
Un-subtracted Coil mass

Clinical IV 3D-DSA (mask + filled scans)



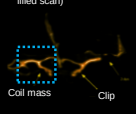
SMART-RECON IV 3D-DSA (only filled scan)

Cleanly subtracted Coil mass



Coil mass

Clip



Coil mass

Clip

- Coil mass and metal clip can be subtracted neatly

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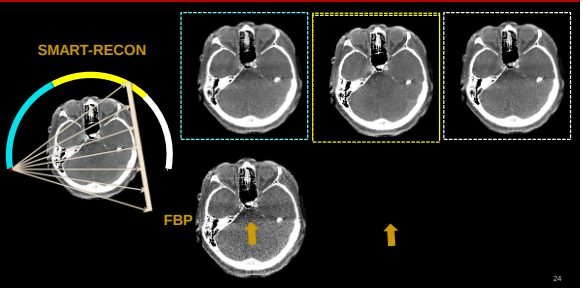
Beam Hardening Artifacts Reduction in SMART-RECON



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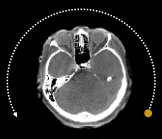
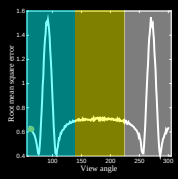
Reduced Beam Hardening Artifacts in SMART-RECON



C-arm CBCT Head Scan



Data inconsistency level vs view angle

A more rapidly changing RMSE indicates a higher level of spectral data inconsistency (e.g. left and right windows) and vice versa (middle window)!

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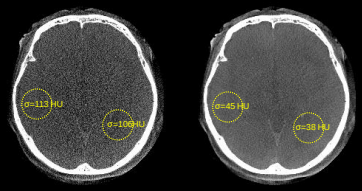
Noise Reduction in SMART-RECON



CNR improved by factor of 2.5~3.0 at the same radiation dose level.

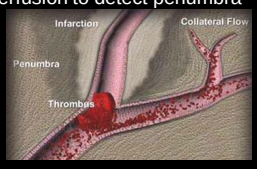
At the same CNR level, SMART-RECON enables further reduction in radiation dose in all cone beam CT scans.

Imaging *needed* in One-Stop-Shop workflow

- Non-contrast whole brain cone beam CT image to exclude hemorrhage;
- Time-resolved CBCT angiography to locate occlusion site and perform collateral analysis;
- Whole brain cone-beam CT Perfusion to detect penumbra and infarction core;

Plus:

- Reduced motion artifacts;
- Reduced radiation dose;
- Reduced beam hardening;
- ……



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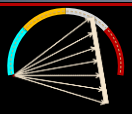
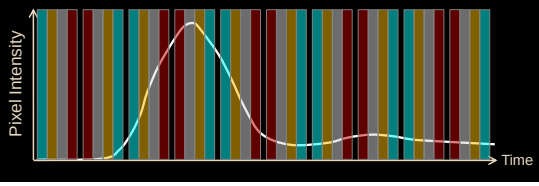
SMART-RECON in C-arm CBCT perfusion

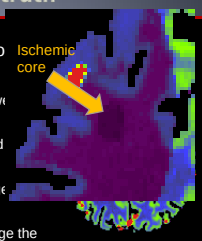


- A factor of four improvement in temporal resolution! (from 6 to 1.5 s)
- A factor of 4 improvement in temporal sampling density (10 points to 40 points)



Validation studies with ground truth

- An anthropomorphic digital perfusion phanto was used
  - Perfusion parameters (CBF, CBV, MTT and TTP) w varied for each tissue voxel
  - The time attenuation curves (TACs) were simulated the user-specified arterial input function (AIF)
  - Low contrast penumbra was introduced to challenge SMART-RECON method
  - An ischemic core was introduced to further challenge the SMART-RECON method

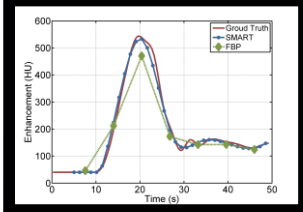


* Manhart et al., IEEE Trans. Med. Imag. 32, 1336 (2013) http://www5.cs.fau.de/research/data/digital-brain-perfusion-phantom/

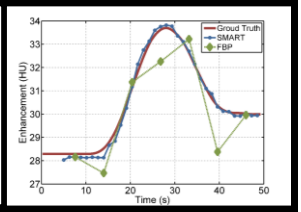
Numerical validation studies: data acquisition

- C-arm CBCTP acquisition was simulated based on the research CBCTP prototype protocol
  - 9 sweeps in total
  - 5.2 s/sweep
  - Pause time: 1.2 s
  - Rotation angular range is 260 degree
- Noise was inserted in the projection domain
- Four time frames were reconstructed from each sweep using SMART-RECON

Contrast uptake curves: artery vs soft tissue

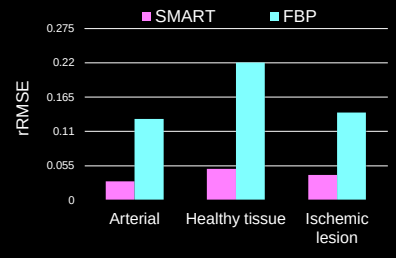


Arterial enhancement curve

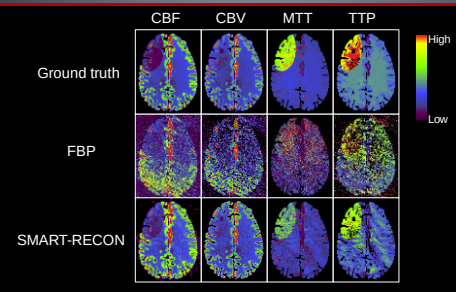


Tissue enhancement curve

Contrast uptake curves: quantitative accuracy



Comparison of perfusion maps



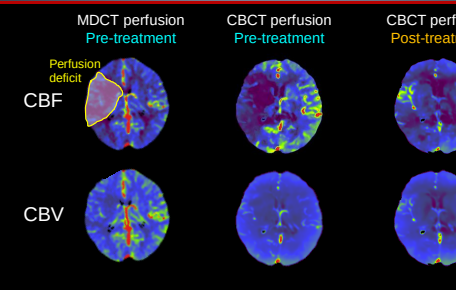
Pilot Clinical Validation Studies

- In collaboration with Drs. Doerfler and Struffert at the University of Erlangen-Nuremberg
- 19 clinical cases were analyzed by far
- Only one sample clinical case will be presented here

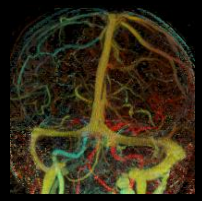
- 87 year old female with RICA occlusion

- MDCT perfusion and CTA imaging acquisition were performed for clinical purpose
- CBCT perfusion acquisition was performed for research purpose right before the revascularization therapy (~4mSv dose)
- CBCT perfusion acquisition was performed again right after the revascularization therapy (~4mSv dose)

Pilot human subject study

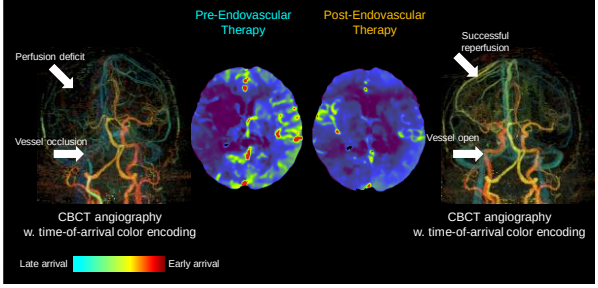


Time-resolved cone beam CT angiography extracted from CBCT perfusion acquisition



Time-of-arrival map

Time-resolved cone beam CT angiography extracted from CBCT perfusion acquisition



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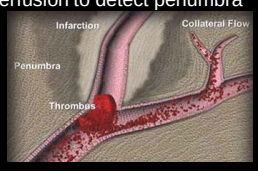

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From SMART-RECON to SMART-Denoise

Image reconstruction problem:
Objective function=Data fitting term and a regularizer/prior model about the image

$$\hat{\mathbf{X}} = \arg\min_{\mathbf{x}} \left[\frac{1}{2} \left(\vec{\mathbf{y}} - \mathbf{A}\vec{\mathbf{X}} \right)^{\mathrm{T}} \mathbf{D} \left(\vec{\mathbf{y}} - \mathbf{A}\vec{\mathbf{X}} \right) + \lambda \| \mathbf{X}_{\mathrm{n}} \|_{\mathrm{n}} \right]$$

Image denoising problem:
Objective function= Image similarity and a regularizer/prior model about the image

$$\hat{X} = \arg\min_{X} \frac{1}{2} \| X - \hat{X} \|^2 + \lambda \| X \|_{\mathrm{n}}$$

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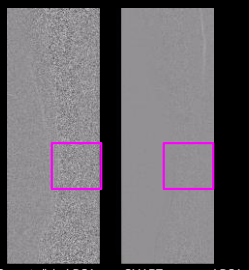
SMART-2D: Clinical case

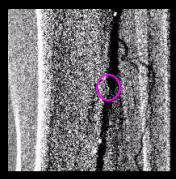
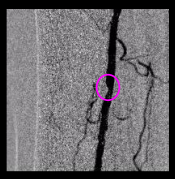
- Data from Germany
- 15 frame/s
- Total 83 frames
- Human leg DSA



Current clinical DSA

SMART processed DSA

SMART-2D: Zoom in movie


Clinical DSA

SMART Processed DSA

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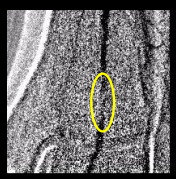
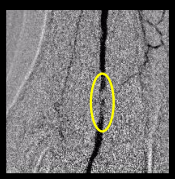
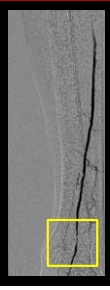
SMART-2D: Zoom in movie

Clinical DSA

SMART Processed DSA

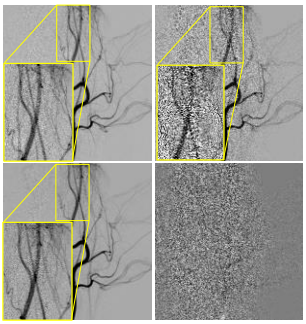
44

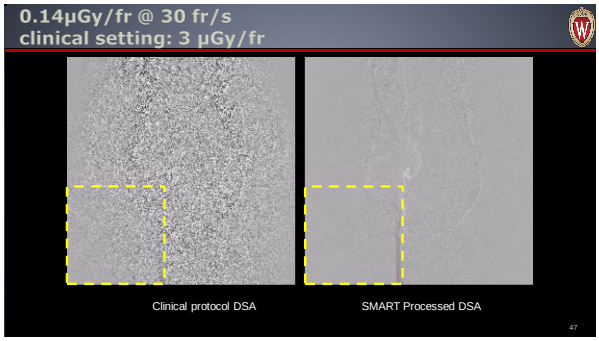
From CNR gain to radiation dose reduction: Canine study to figure out radiation dose reduction

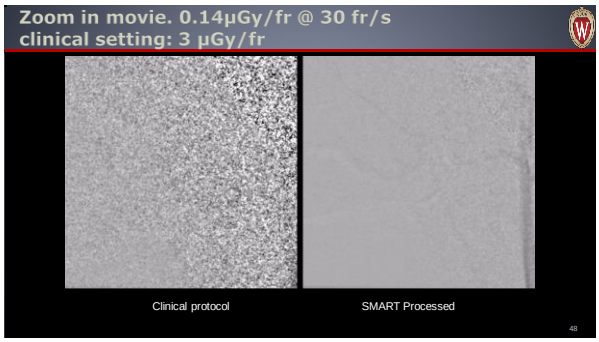
- DSA images were obtained using the following dose settings:
  - 3 µGy/frame (clinical setting), 0.36 µGy/frame, 0.14 µGy/frame
- 50% and 25% contrast concentration injections
- Frame rate: 30 frame/second
- Siemens Artis Zee biplane system

	Delay (s)	Volume (ml)	Concentration (%)	Flow (ml/s)	Injection time (s)
50% concentration level	1	6	50	2	3
25% concentration level	1	8	25	2	4

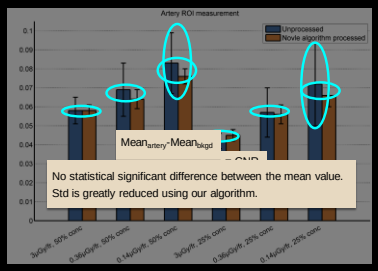
45




0.14µGy/fr @ 30 fr/s
clinical setting: 3 µGy/fr
Clinical protocol DSA
SMART Processed DSA
47

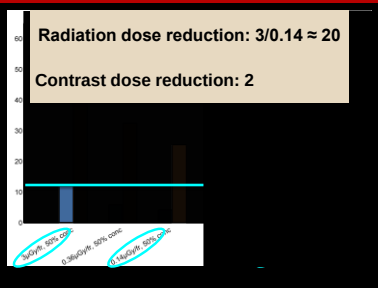

Zoom in movie. 0.14µGy/fr @ 30 fr/s
clinical setting: 3 µGy/fr
Clinical protocol
SMART Processed
48

Artery ROI measurement



49

Contrast to noise



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Outline

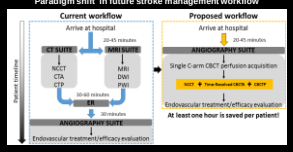
- Technical challenges and technical solution, SMART-RECON, to address the challenges
- SMART-3D: generate 3D DSA and soft tissue images with reduced motion artifacts, beam hardening artifacts and noise level from a single sweep cone-beam CT (CBCT) acquisition
- SMART-4D: generate time-resolved CBCT angiography and whole brain CBCT perfusion maps
- SMART-2D in angio suite: factor of 20 reduction of radiation dose in 2D DSA
- Summary

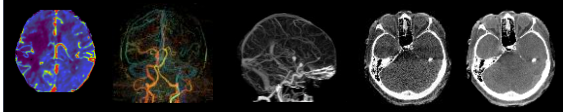
SMART-RECON related imaging techniques

Enabling multi-modality imaging in Angio-suite

- SMART-RECON enables a factor of 4 times improvement in temporal resolution to enable simultaneous whole brain cone beam CT perfusion imaging and time-resolved cone-beam CT angiography in Angio suites
- SMART-RECON enables IV-3D DSA from a single acquisition with reduced motion artifacts and reduced radiation dose.
- SMART-RECON enables cone-beam CT imaging for brain soft tissues with reduced beam-hardening artifacts and reduced noise.
- SMART-RECON inspires CNR enhancement and radiation dose reduction in routine 2D-DSA exams

Paradigm shift in future stroke management workflow





CBCT Perfusion | 4D CBCT Angiogram | IV-3D DSA w/o mask scan | CBCT with reduced artifacts and noise

Thank You

Canine study ROI measurement

ROI on the artery

ROI on a uniform region close to artery

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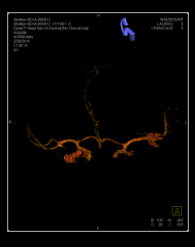
Current clinical workflow

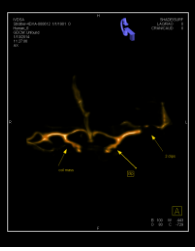
Thank You

Improved visualization of coil and clip subtraction

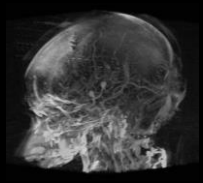
Clinical IV 3D-DSA



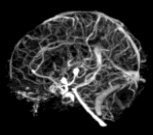
SMART IV 3D-DSA



Clinical example: 3D DSA images (MIP)



Clinical IV 3D-DSA



SMART IV 3D-DSA

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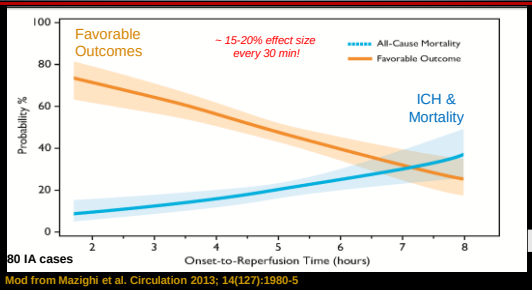
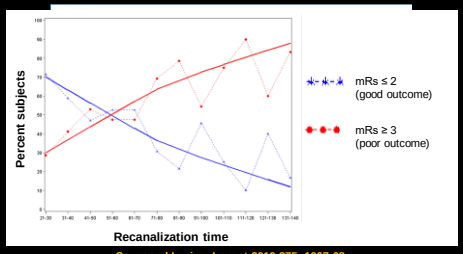
Time to Reperfusion: Outcome and Mortality



80 IA cases

Mod from Mazighi et al. Circulation 2013; 14(127):1980-5

The golden hour of stroke intervention



Saver and Levine, Lancet 2013; 376: 1567-68

Spiotta A et. al. JNIS 2014:6:511-516

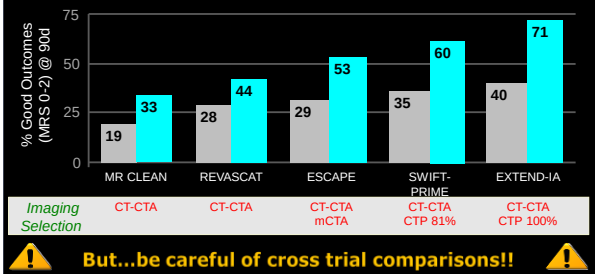
Even with great effort, critical time is lost in stroke protocols which employ multi-modality imaging

- Procedure characteristics in EXTEND-IA Trial
  - ONSET TO GROIN PUNCTURE 210 (166-251)
  - **CT TO GROIN PUNCTURE 93 (71-138)**
  - GROIN PUNCTURE TO TICI 2B/3 OR COMPLETION 43 (24-53)
  - ONSET TO TICI 2B/3 OR COMPLETION 248 (204-277)

Positive IV→ IA stroke trials in 2015

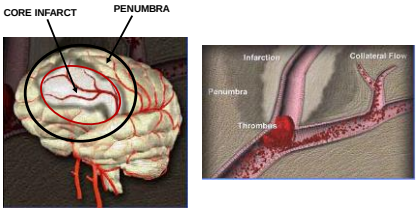
Trial	Treatment Timeline	Imaging Selection	Outcome IV Only	Outcome IV + IA
MR CLEAN N= 500 Berkhemer NEJM 2015	IV TPA by 4.5 hrs Wait for response Start IA by 6 hrs Puncture @ 260 min	CT - ASPECTS 7-10 CTA - Anterior clot CTP - done in 65% - details not reported	MRS 0-2: 19% Recan: 33%	MRS 0-2: 33% Recan: 75%
ESCAPE N= 316 Goyal NEJM 2015	Symptoms 0-12 hrs IV TPA by 4.5 hrs Puncture @ 185 min CT-reperfusion 84m	CT - ASPECTS 6-10 CTA - Anterior clot mCTA ≥ 50% MCA	MRS 0-2: 29% Recan: 37%	MRS 0-2: 53% Recan: 72%
EXTEND IA N= 70 Campbell NEJM 2015	IV TPA by 4.5 hrs → +/- IA by 6 hours Puncture @ 210 min	CT – IV TPA criteria CTA - Anterior clot CTP - 25% excluded Tmax >6s, rCBF<30%	MRS 0-2: 40% Recan: 34%	MRS 0-2: 71% Recan: 100%
SWIFT-PRIME N= 196 Saver NEJM 2015	IV TPA by 4.5 hrs → +/- IA Solitaire by 6h Puncture @ 224 min	CT – ASPECTS 7-10 CTA - Anterior Clot CTP - Target MM 84% Exclude malignant 13%	MRS 0-2: 35% Recan: N/A	MRS 0-2: 60% Recan: 88%
REVASCAT N= 206 Jovin NEJM 2015	IV TPA by 4.5 hrs → Wait 30 min; CTA/MRA +/- IA Solitaire by 8h Puncture @ 269 min	CT – ASPECTS 7-10 DWI - ASPECTS ≥ 5 CTA/MRA - Anterior Clot	MRS 0-2: 28% Recan: N/A	MRS 0-2: 44% Recan: 66%

Endovascular trials in 2015: Good outcomes with advanced imaging selection

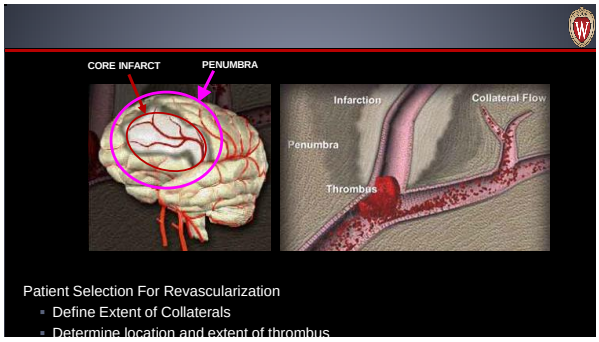


But…be careful of cross trial comparisons!!

THE ISCHEMIC CORE AND PENUMBRA



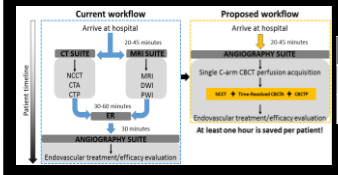
PENUMBRA = A SURROUNDING OR ADJOINING REGION IN WHICH SOMETHING EXISTS IN A LESSER DIGREE (FRINGE)



Patient Selection For Revascularization

- Define Extent of Collaterals
- Determine location and extent of thrombus

Proposal: One-Stop-Shop imaging workflow



	Door to groin puncture time	Typical radiation dose
Current workflow	2-2.5 Hrs.	6-9 mSv
Proposed One Stop Shop workflow	<1 Hr.	4.6 mSv

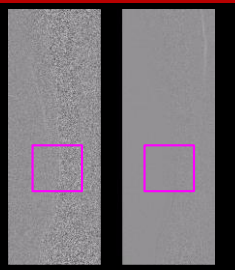
References:
1. Diekmannet at al., AJNR 2010; 31: 1003
2. Abels et al., AJNR 2011; 32: 1632
3. Yang et al., Stroke 2015; 46: 3383

Outline

- Clinical background and motivations for one-stop-shop imaging
- Technical challenges and new technical solution: SMART-RECON technology
- SMART-4D in angio suite: Whole brain perfusion and time-reolsoved angiography
- SMART-3D in angio suite: Maskless 3D IV-DSA with reduced motion artifacts, beam hardening artifacts and radiation dose
- SMART-2D in angio suite: factor of 20 reduction of radiation dose in 2D DSA
- Summary

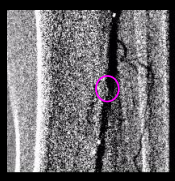
SMART-2D: Image quality improvement in 2D-DSA

- Data from Germany
- 15 frame/s
- Total 83 frames
- Human leg DSA

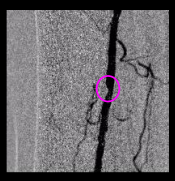


Clinical DSA image SMART processed image

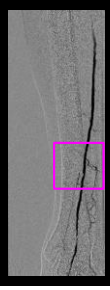
Zoom in movie



Undenoised



SMART denoised



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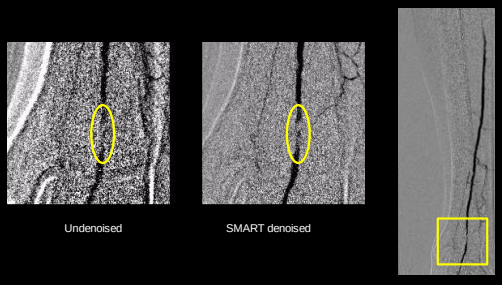
Zoom in movie



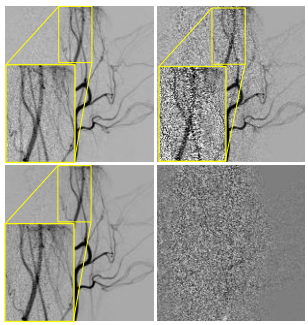
70

Improved image quality at normal dose means radiation dose reduction potential, but how much?

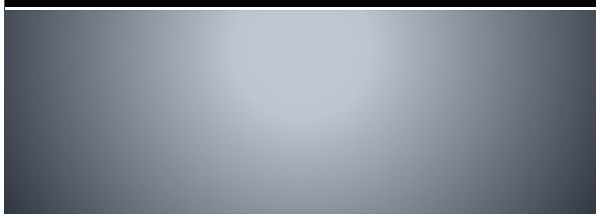
- DSA images were obtained using the following dose settings:
  - 3 µGy/frame (clinical setting), 0.36 µGy/frame, 0.14 µGy/frame
- 50% and 25% contrast concentration injections
- Frame rate: 30 frame/second
- Siemens Artis Zee biplane system

	Delay (s)	Volume (ml)	Concentration (%)	Flow (ml/s)	Injection time (s)
50% concentration level	1	6	50	2	3
25% concentration level	1	8	25	2	4

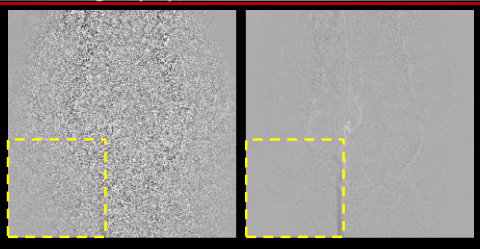
71



Movies



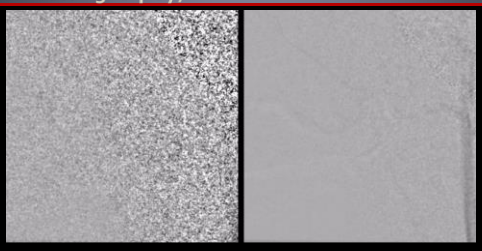
0.14μGy/fr @ 30 fr/s
clinical setting: 3 μGy/fr



Undenoised SMART denoised

74

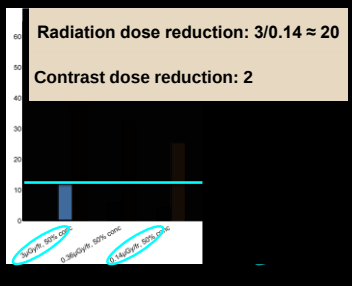
Zoom in movie. 0.14μGy/fr @ 30 fr/s
clinical setting: 3 μGy/fr



Undenoised SMART denoised

75

Contrast to noise



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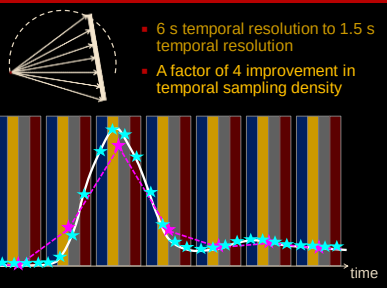
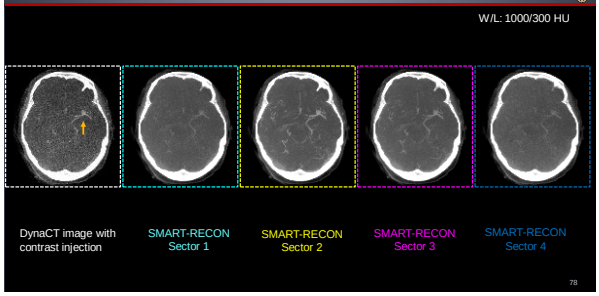
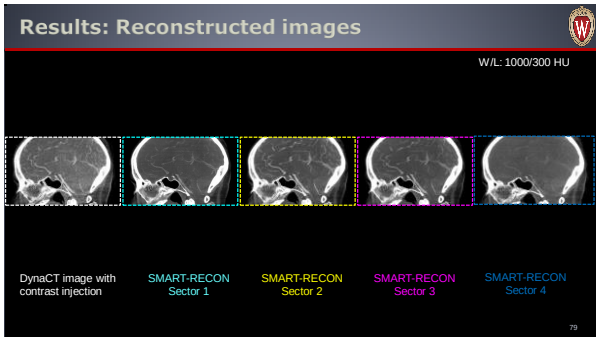
SMART-RECON in CBCT perfusion

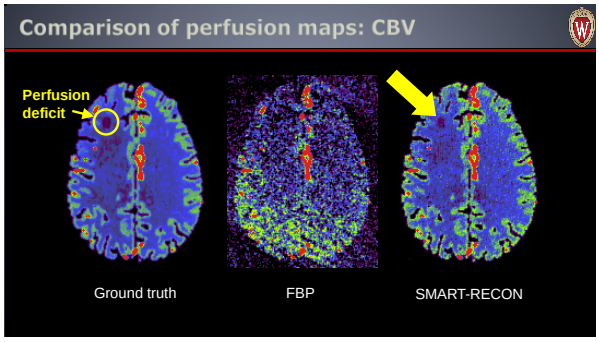


Clinical example: Reconstructed Images



78


Results: Reconstructed images
W/L: 1000/300 HU
DynaCT image with contrast injection
SMART-RECON Sector 1
SMART-RECON Sector 2
SMART-RECON Sector 3
SMART-RECON Sector 4
79


Comparison of perfusion maps: CBV
Perfusion deficit
Ground truth
FBP
SMART-RECON