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

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## Acknowledgement

UW-Madison Stroke Imaging Research Team:

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

Members (Basic Science):

Dr. Ke Li, Dr. Yijing Wu, Yinsheng Li, John Garrett, Kai Niu

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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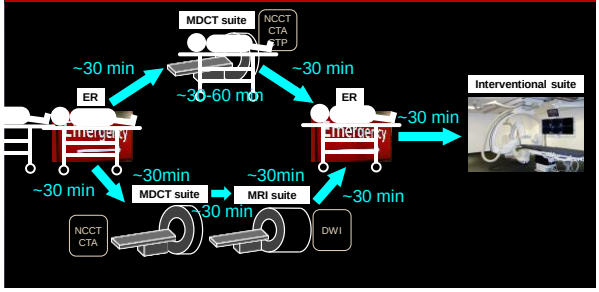
## Clinical motivations: Current clinical workflow for acute ischemic stroke patients

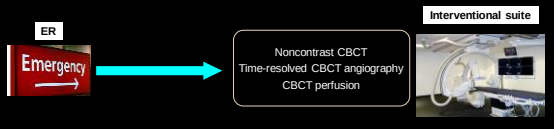


## Procedure characteristic in published clinical trials

- 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

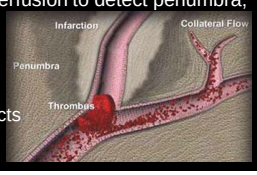



## Imaging *needed* in One-Stop-Shop workflow

- 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

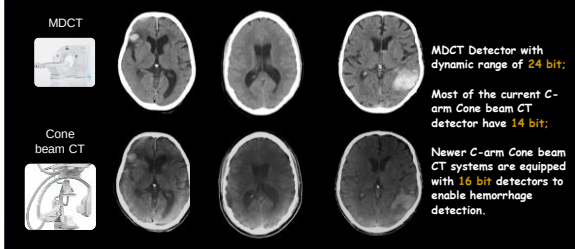



Image courtesy of Prof. Skalej, Neuroradiology, Magdeburg. Image acquired with Siemens Artis Q.

## Imaging *needed* in One-Stop-Shop workflow

- Non-contrast whole brain cone beam CT image to detect hemorrhage; ✓
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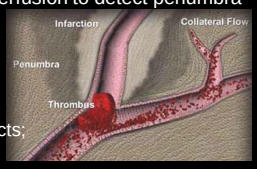
- Whole brain cone-beam CT Perfusion to detect penumbra and infarction core;

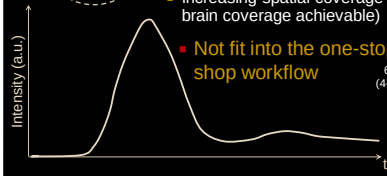
Plus:

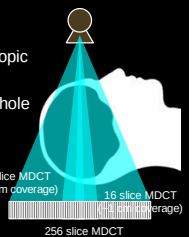
- Reduced motion artifacts;
- Reduced radiation dose;
- Reduced beam hardening artifacts;
- ……



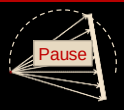

## MDCT perfusion imaging: State-of-the-art

- 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

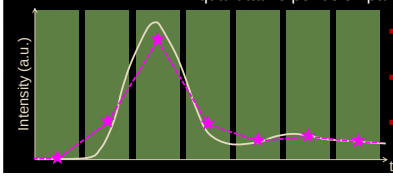


## Cone beam CT perfusion: Idea and Challenges

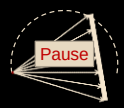



- Low temporal sampling density: from few data points (7-10) to recover contrast uptake curve;
- Low temporal resolution: from temporally averaged inaccurate measurements to obtain quantitative perfusion parameters.




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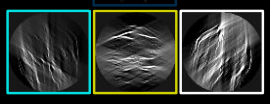
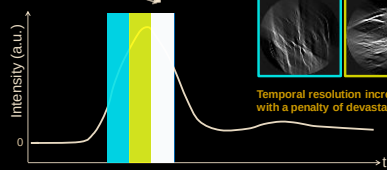
## Small angular sector to increase temporal resolution: A very simple idea

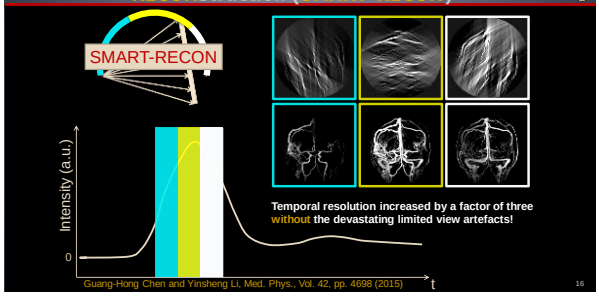
Conventional Filtered Backprojection (FBP) Reconstruction






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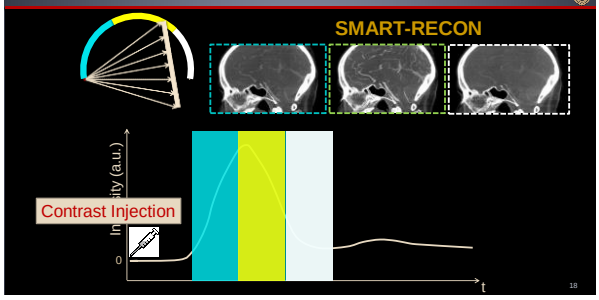
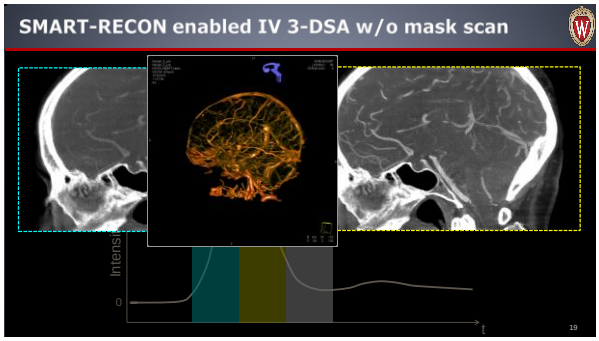
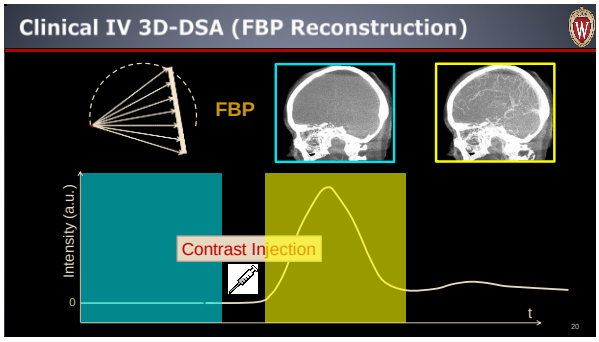
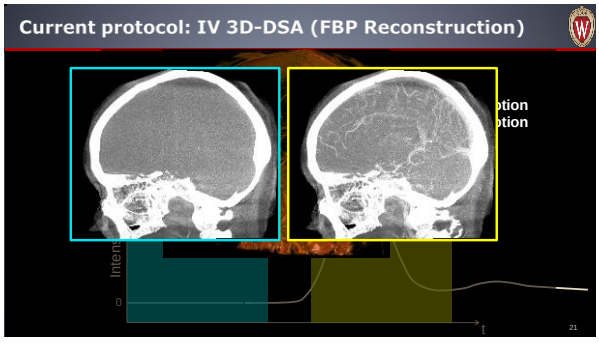
## SMART-RECON enabled IV 3D-DSA w/o mask scan

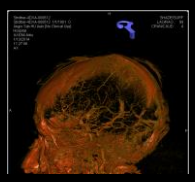


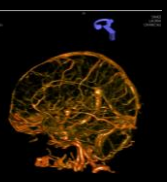

SMART-RECON enabled IV 3-DSA w/o mask scan
Intens
0
t
19


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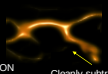
## Clinical IV 3D-DSA vs SMART-RECON IV 3D-DSA

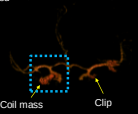
Un-subtracted Coil mass

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



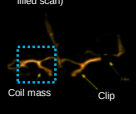
SMART-RECON IV 3D-DSA (only filled scan)

Cleanly subtracted Coil mass



Coil mass

Clip



Coil mass

Clip

- Coil mass and metal clip can be subtracted neatly

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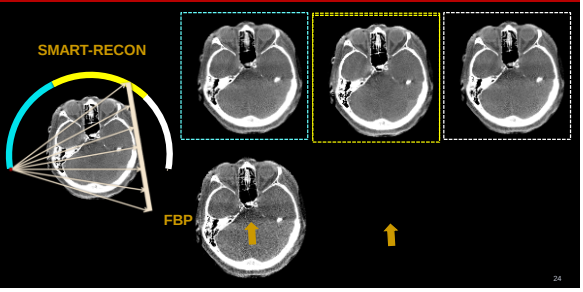
## Beam Hardening Artifacts Reduction in SMART-RECON

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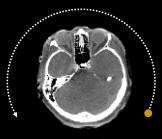
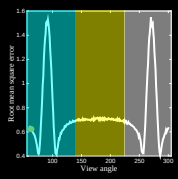
## Reduced Beam Hardening Artifacts in SMART-RECON



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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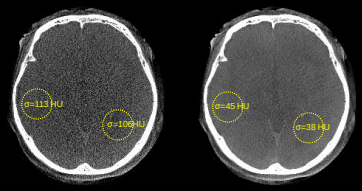
## Noise Reduction in SMART-RECON




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

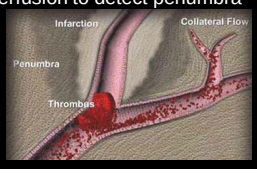
At the same CNR level, SMART-RECON enables further reduction in radiation dose in all cone beam CT scans.

## 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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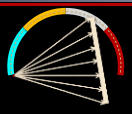
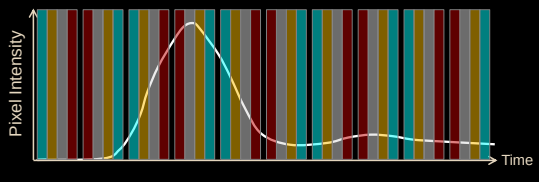
## SMART-RECON in C-arm CBCT perfusion

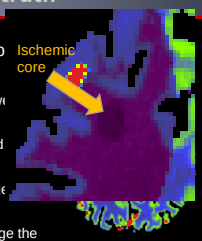


- A factor of four improvement in temporal resolution! (from 6 to 1.5 s)
- A factor of 4 improvement in temporal sampling density (10 points to 40 points)




## 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

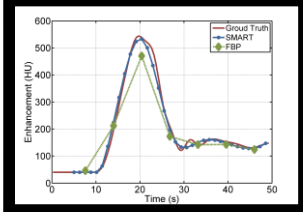



* Manhart et al., IEEE Trans. Med. Imag. 32, 1336 (2013) http://www5.cs.fau.de/research/data/digital-brain-perfusion-phantom/

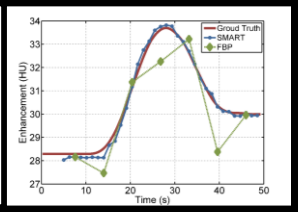
## Numerical validation studies: data acquisition

- 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

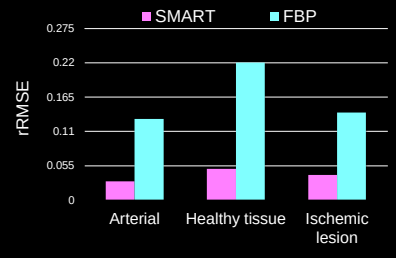



Arterial enhancement curve

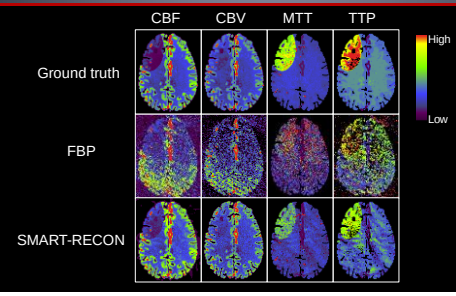



Tissue enhancement curve

## Contrast uptake curves: quantitative accuracy



## Comparison of perfusion maps



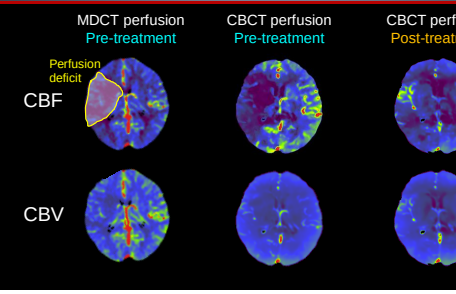

## Pilot Clinical Validation Studies

- 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

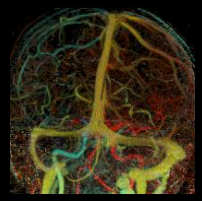
- 87 year old female with RICA occlusion

- 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

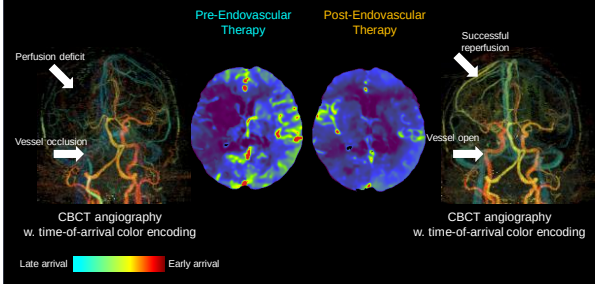


## Time-resolved cone beam CT angiography extracted from CBCT perfusion acquisition




Time-of-arrival map

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

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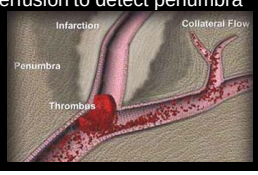

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## From SMART-RECON to SMART-Denoise

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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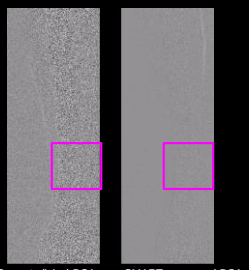
## SMART-2D: Clinical case

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

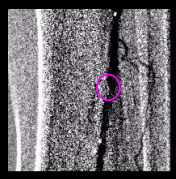
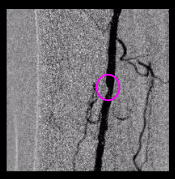


Current clinical DSA



SMART processed DSA

## SMART-2D: Zoom in movie


Clinical DSA

SMART Processed DSA

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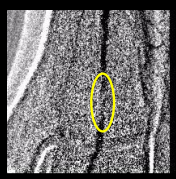
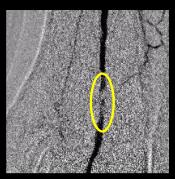
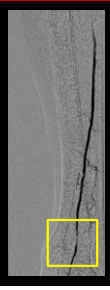
## SMART-2D: Zoom in movie

Clinical DSA

SMART Processed DSA

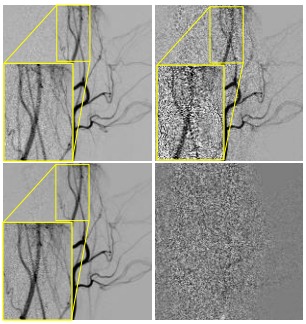
44

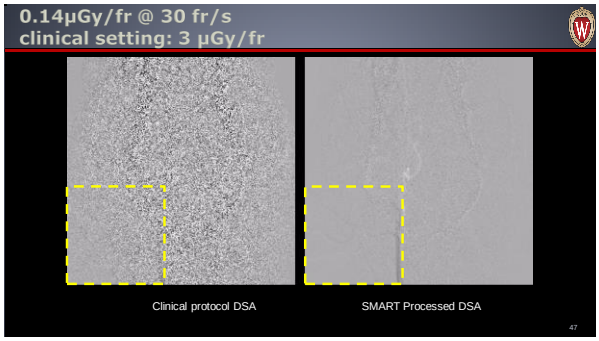
## From CNR gain to radiation dose reduction: Canine study to figure out radiation dose reduction

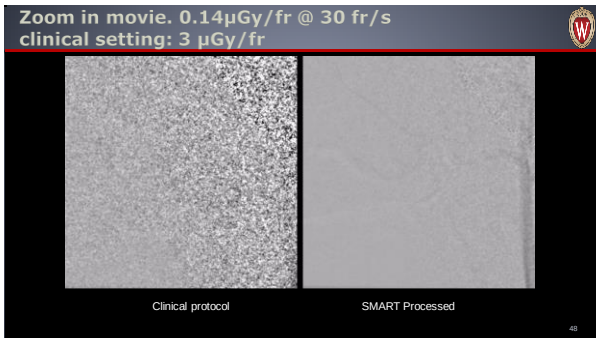
- DSA images were obtained using the following dose settings:
  - 3 µGy/frame (clinical setting), 0.36 µGy/frame, 0.14 µGy/frame
- 50% and 25% contrast concentration injections
- Frame rate: 30 frame/second
- Siemens Artis Zee biplane system

| | 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 |

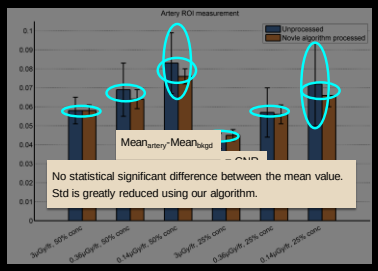
45




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

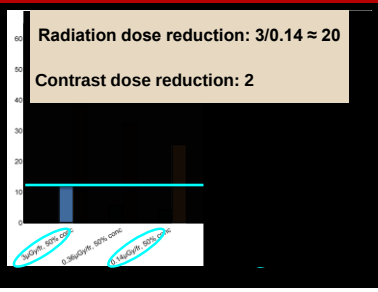

Zoom in movie. 0.14µGy/fr @ 30 fr/s
clinical setting: 3 µGy/fr
Clinical protocol
SMART Processed
48

## Artery ROI measurement




49

## Contrast to noise

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## Outline

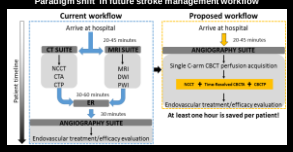
- Technical challenges and technical solution, SMART-RECON, to address the challenges
- SMART-3D: generate 3D DSA and soft tissue images with reduced motion artifacts, beam hardening artifacts and noise level from a single sweep cone-beam CT (CBCT) acquisition
- SMART-4D: generate time-resolved CBCT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

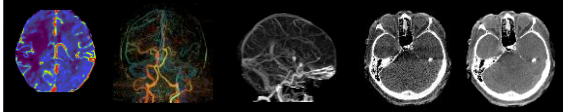
## SMART-RECON related imaging techniques

**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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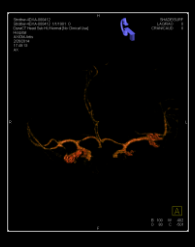
## Current clinical workflow

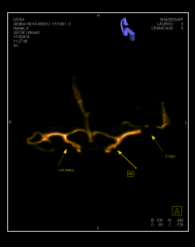
## Thank You

## Improved visualization of coil and clip subtraction

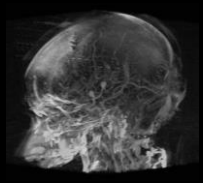
Clinical IV 3D-DSA



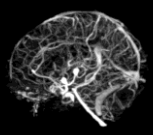
SMART IV 3D-DSA



## Clinical example: 3D DSA images (MIP)



Clinical IV 3D-DSA



SMART IV 3D-DSA

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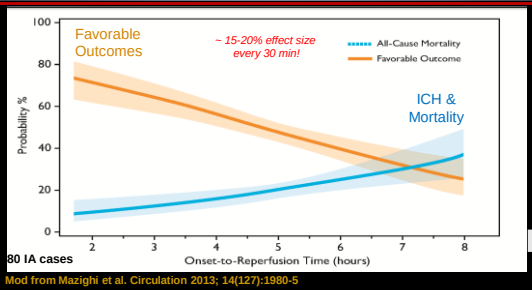
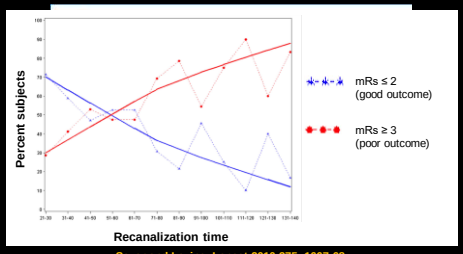
## Time to Reperfusion: Outcome and Mortality




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

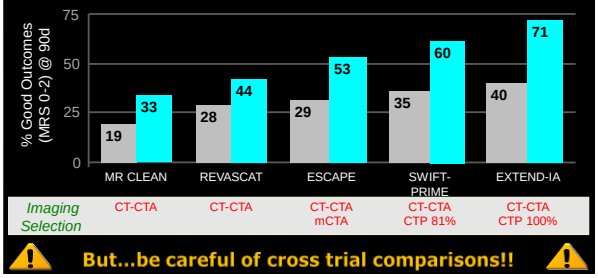
## Even with great effort, critical time is lost in stroke protocols which employ multi-modality imaging

- 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

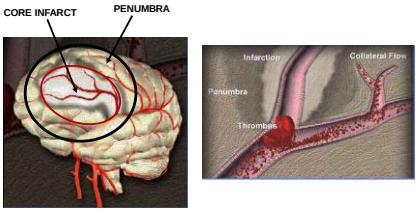
| Trial | Treatment Timeline | Imaging Selection | Outcome IV Only | Outcome IV + IA |
|---|---|---|---|---|
| *MR CLEAN*<br>N= 500<br>Berkhemer<br>NEJM 2015 | IV TPA by 4.5 hrs<br>Wait for response<br>Start IA by 6 hrs<br>Puncture @ 260 min | CT - ASPECTS 7-10<br>CTA - Anterior clot<br>CTP - done in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

## Endovascular trials in 2015: Good outcomes with advanced imaging selection

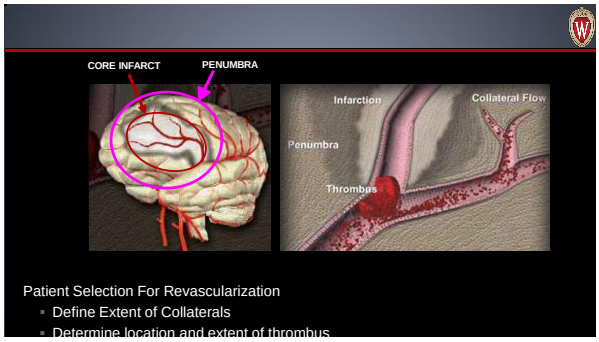



**But…be careful of cross trial comparisons!!**

## THE ISCHEMIC CORE AND PENUMBRA



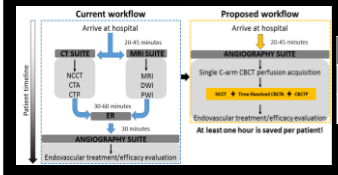

PENUMBRA = A SURROUNDING OR ADJOINING REGION IN WHICH SOMETHING EXISTS IN A LESSER DIGREE (FRINGE)




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 |

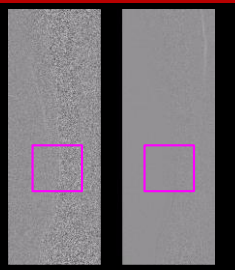
References:
1. Diekmannet at al., AJNR 2010; 31: 1003
2. Abels et al., AJNR 2011; 32: 1632
3. Yang et al., Stroke 2015; 46: 3383

## 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

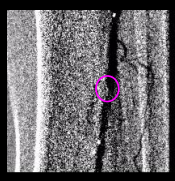
## SMART-2D: Image quality improvement in 2D-DSA

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

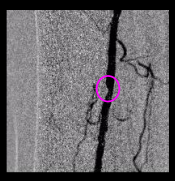


Clinical DSA image SMART processed image

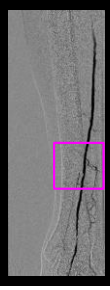
## Zoom in movie



Undenoised



SMART denoised



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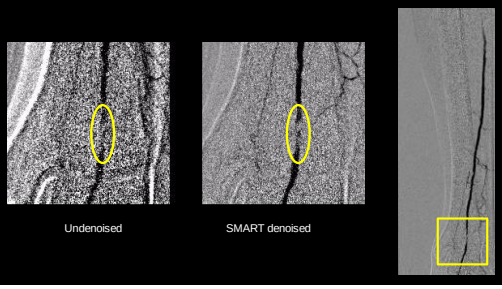
## Zoom in movie



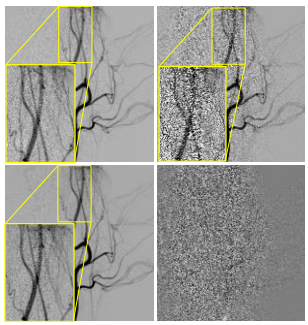

70

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

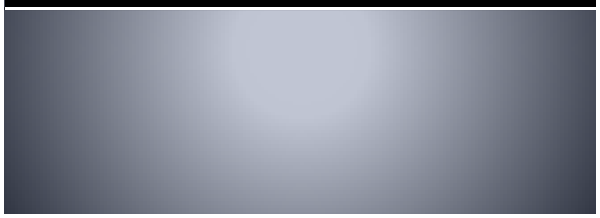
- DSA images were obtained using the following dose settings:
  - 3 µGy/frame (clinical setting), 0.36 µGy/frame, 0.14 µGy/frame
- 50% and 25% contrast concentration injections
- Frame rate: 30 frame/second
- Siemens Artis Zee biplane system

| | 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 |

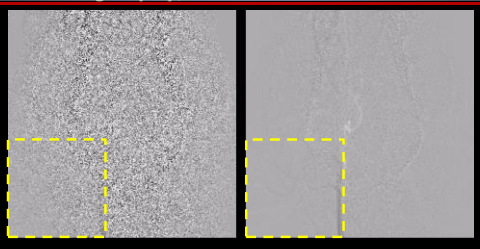
71



## Movies



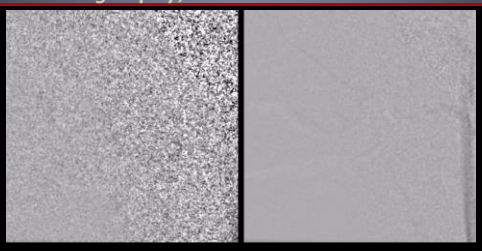
## 0.14μGy/fr @ 30 fr/s
## clinical setting: 3 μGy/fr



Undenoised SMART denoised

74

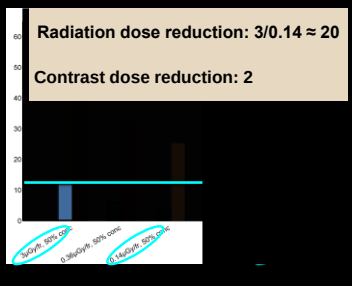
## Zoom in movie. 0.14μGy/fr @ 30 fr/s
## clinical setting: 3 μGy/fr



Undenoised SMART denoised

75

## Contrast to noise

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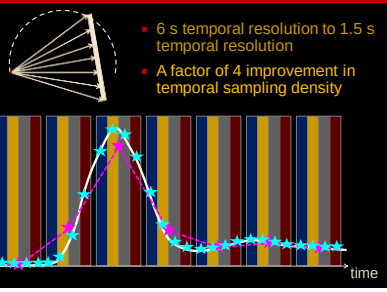
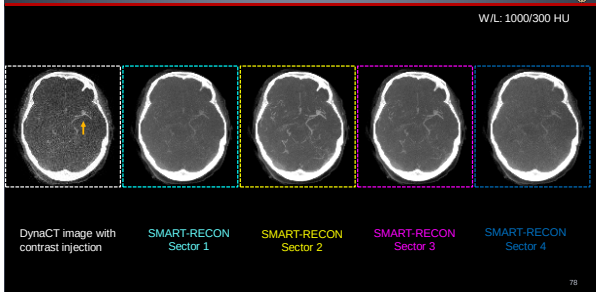
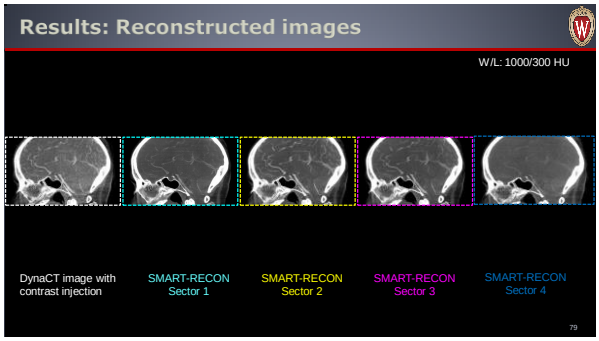
## SMART-RECON in CBCT perfusion

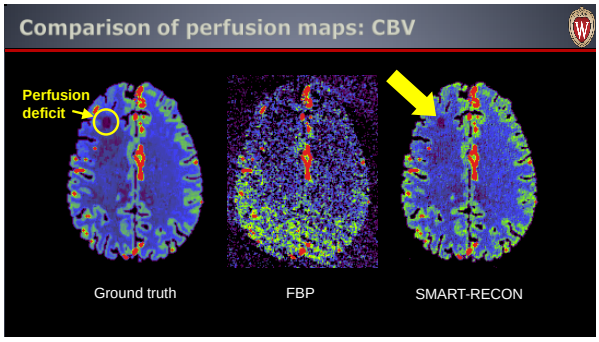



## Clinical example: Reconstructed Images




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