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

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

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

Non-contrast whole brain cone beam CT image to detect hemorrhage;
- Reduced radiation dose;
- Reduced beam hardening artifacts

Plus:
- Time-resolved CBCT angiography to locate occlusion site and collaterals;
- Whole brain cone-beam CT Perfusion to detect penumbra;
Cone beam CT

- MDCT Detector with dynamic range of 24 bit.
- Most of the current C-arm Cone beam CT detector have 14 bit.
- Newer C-arm Cone beam CT systems are equipped with 16 bit detectors to enable hemorrhage detection.

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**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**

- 64 slice MDCT (~1 cm coverage)
- 16 slice MDCT (~4 cm coverage)
- 256 slice MDCT (~16 cm coverage)
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

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

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 artifacts!
Temporal resolution increased by a factor of three without the devastating limited view artefacts!

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

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

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

- Coil mass and metal clip can be subtracted neatly

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

Beam Hardening Artifacts Reduction in SMART-RECON

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

C-arm CBCT Head Scan

Data inconsistency level vs view angle

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.

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

  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

<table>
<thead>
<tr>
<th></th>
<th>SMART</th>
<th>FBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic lesion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

rRMSE

0.275

0.22

0.165

0.11

0.055

0
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)
Time-resolved cone beam CT angiography extracted from CBCT perfusion acquisition

Early arrival
Late arrival
Time-of-arrival map

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

Pre-Endovascular Therapy
Post-Endovascular Therapy
Successful reperfusion

Vessel occlusion
CBCT angiography w. time-of-arrival color encoding

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;
- ……
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
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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

\[ X = \arg \min \left[ \| y - Ax \|^2 + \lambda \| X \|^2 \right] \]

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

\[ X = \arg \min \left[ \| \begin{bmatrix} \mathbf{x}^1 \\ \mathbf{x}^2 \end{bmatrix} - \begin{bmatrix} \mathbf{y}^1 \\ \mathbf{y}^2 \end{bmatrix} \|^2 + \lambda \| \begin{bmatrix} \mathbf{x}^1 \\ \mathbf{x}^2 \end{bmatrix} \|^2 \right] \]

SMART-2D: Clinical case

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

<table>
<thead>
<tr>
<th>Delay (s)</th>
<th>Volume (ml)</th>
<th>Concentration (%)</th>
<th>Flow (mL/s)</th>
<th>Injection time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% concentration level</td>
<td>1</td>
<td>6</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>20% concentration level</td>
<td>1</td>
<td>8</td>
<td>25</td>
<td>2</td>
</tr>
</tbody>
</table>
No statistical significant difference between the mean value. Std is greatly reduced using our algorithm.

Radiation dose reduction: $\frac{3}{0.14} \approx 20$

Contrast dose reduction: 2

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
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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 improves CBF, CBFV, and intracranial venous blood flow imaging with improved spatial resolution.
- SMART-RECON improves CNR enhancement and radiation dose reduction in routine 2D DSA exams.

ROI on the artery
ROI on a uniform region close to artery

Thank You

Canine study ROI measurement
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

Time to Reperfusion: Outcome and Mortality

- Favorable Outcomes: ~15-20% effect size every 30 min!
- ICH & Mortality

The golden hour of stroke intervention

- mRS ≤ 2 (good outcome)
- mRS ≥ 3 (poor outcome)
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 (34-53)
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### Positive IV→IA stroke trials in 2015

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment Timeline</th>
<th>Imaging Selection</th>
<th>Outcome IV Only</th>
<th>Outcome IV + IA</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN</td>
<td>IV TPA by 4.5 hrs</td>
<td>CT - ASPECTS 7-10</td>
<td>MRS 0-2: Recan: 35%</td>
<td>MRS 0-2: Recan: 55%</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>Symptom onset IV TPA by 4.5 hrs CTA @ 195 min</td>
<td>CT - ASPECTS 6-10 CTA - Anterior clot mCTA ≥ 50%</td>
<td>MRS 0-2: Recan: 35%</td>
<td>MRS 0-2: Recan: 55%</td>
</tr>
<tr>
<td>EXTEND IA</td>
<td>IV TPA by 4.5 hrs</td>
<td>CT - IV TPA criteria CTA - Anterior clot CTP &gt; 25%</td>
<td>MRS 0-2: Recan: 55%</td>
<td>MRS 0-2: Recan: 100%</td>
</tr>
<tr>
<td>SWIFT-PRIME</td>
<td>IV TPA by 4.5 hrs</td>
<td>CT - ASPECTS 7-10 CTA - Anterior clot CTP ≥ 50%</td>
<td>MRS 0-2: Recan: 55%</td>
<td>MRS 0-2: Recan: 100%</td>
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<td>REVASCAT</td>
<td>IV TPA by 4.5 hrs</td>
<td>CT - ASPECTS 7-10 CTA - Anterior clot</td>
<td>MRS 0-2: Recan: 55%</td>
<td>MRS 0-2: Recan: 100%</td>
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### Endovascular trials in 2015: Good outcomes with advanced imaging selection

- MR CLEAN
- REVASCAT
- ESCAPE
- SWIFT-PRIME
- EXTEND-IA

- % Good Outcomes (MRS 0-2 @ 90d)
  - MR CLEAN: 33%
  - REVASCAT: 29%
  - ESCAPE: 44%
  - SWIFT-PRIME: 53%
  - EXTEND-IA: 60%

### Imaging Selection

- CT-CTA
- CT-CTA
- CT-CTA
- CT-CTA
- CT-CTA

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 DEGREE (FRINGE)

Patient Selection For Revascularization
- Define Extent of Collaterals
- Determine location and extent of thrombus

Proposal: One-Stop-Shop imaging workflow

<table>
<thead>
<tr>
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<th>Current workflow</th>
<th>Proposed One-Stop Shop workflow</th>
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<tr>
<td>Door to groin puncture</td>
<td>2-2.5 hrs.</td>
<td>&lt;1 hr.</td>
</tr>
<tr>
<td>Radiation dose</td>
<td>6-9 mSv</td>
<td>4.6 mSv</td>
</tr>
</tbody>
</table>

References:
1. Diekmann et al., AJNR 2010; 31: 1003
2. Abels et al., AJNR 2011; 32: 1632
3. Yang et al., Stroke 2015; 46: 3383
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-resolved 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 frames/s
- Total 83 frames
- Human leg DSA

Zoom in movie

Undenoised SMART denoised
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

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Movies

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

Undenoised SMART denoised

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

Undenoised SMART denoised
Radiation dose reduction: \( \frac{3}{0.14} \approx 20 \)

Contrast dose reduction: 2

- 6 s temporal resolution to 1.5 s temporal resolution
- A factor of 4 improvement in temporal sampling density

W/L: 1000/300 HU

Dynamic image with contrast injection

SMART-RECON Sector 1

SMART-RECON Sector 2

SMART-RECON Sector 3

SMART-RECON Sector 4
**Results: Reconstructed images**

- **DynaCT image with contrast injection**
- **SMART-RECON Sector 1**
- **SMART-RECON Sector 2**
- **SMART-RECON Sector 3**
- **SMART-RECON Sector 4**

**Comparison of perfusion maps: CBV**

- **Perfusion deficit**
- **Ground truth**
- **FBP**
- **SMART-RECON**