Microbubble Super-Localisation in Human Lower Limb Microvasculature with Motion Correction

Sevan Harput, Kirsten Christensen-Jeffries, Yuanwei Li, Jemma Brown, Paul Aljabar, Robert J. Eckersley, Christopher Dunsby and Meng-Xing Tang
Ultrasound Super-Resolution or Super-Localisation

Ideal Case:
- Ultrafast plane wave imaging
- Acquisition of RF or IQ data
- No motion
- Spatially isolated microbubbles

Practical Case:
- Linear scan with a commercial scanner
- Grey scale video. No RF data.
- Motion
- Multiple non-isolated microbubbles

**In-vivo Ultrasound Super-Resolution**

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Motion is an inherent part of diagnostic imaging.
Imaging of Micro-circulation with a commercial scanner

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Sub-optimal super-resolution imaging with a clinical scanner may still help the practitioners to diagnose certain cases.

Human Lower Limb - Tibialis Anterior Muscle

Figure: http://is.muni.cz/do/1451/e-learning/kineziologie/elportal/img/tibialis_anterior.png
Figure: https://web.archive.org/web/20041209023150/http://education.yahoo.com/reference/gray/subjects/subject?id=160
**Focus:** Peripheral artery disease (PAD) is a type of atherosclerosis. It occurs most often in the legs arteries and interferes with the blood circulation in the limb.

**Aim:** To identify the presence of Claudication and Diabetes using contrast enhanced ultrasound imaging.

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Hypothesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Healthy Volunteers</td>
<td>Large difference in microvascular flow before and after exercise</td>
</tr>
<tr>
<td>2 - Claudication</td>
<td>Small difference in microvascular flow before and after exercise</td>
</tr>
<tr>
<td>3 - Diabetes</td>
<td>Almost no difference in microvascular flow before and after exercise</td>
</tr>
</tbody>
</table>

Arteries become narrowed and blood flow decreases in arteriosclerosis.

![Arteries impacted by PAD](http://www.adameducation.com)
CEUS imaging of human lower limb
Motion Estimation & Correction (rigid) → Motion Estimation (non-rigid registration)

Motion Correction (rigid) → Motion Correction (non-rigid)

Transformation Matrix

Spatio-temporal Filtering

Noise Threshold (depth-dependent)

MB detection

Super-Localization

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Rigid Motion Estimation & Correction

2D rigid sub-pixel cross-correlation with a reference frame.

Up-sampling with bicubic interpolation from the original pixel scale.

Error (regarding to the reference frame)

Rigid Motion Correction
Sum of Squared Differences ($\mu = 0.007$)

Mean SSD = 0.007

Non-Rigid Motion Correction
Sum of Squared Differences ($\mu = 0.004$)

Mean SSD = 0.004
Maximum Intensity Projection of all frames

580 frames = 45 seconds
Maximum Intensity Projection of all frames

580 frames = 45 seconds
Super-Localisation

580 frames = 45 seconds
Super-Localisation

All MB events (number of counts)

All MB events (number of counts) with Motion Correction
Effect of Motion Correction on Micro-vasculature

No Motion Correction vs. With Motion Correction in different depth and lateral dimensions.
Effect of Motion Correction on Micro-vasculature
Motion Correction

**B-mode Original 1**

**B-mode (Motion Corrected)**

- Depth (mm): 8 to 23
- Lateral (mm): 8 to 15
Comparison - Micro-vessel thickness

Maximum Intensity Projection (MIP)  
Super-Localised Microbubbles (SLM)

Maximum Intensity Projection (MIP)  
Super-Localised Microbubbles (SLM) with Motion Correction

no Motion Correction

with Motion Correction

Normalised Amplitude

Lateral distance (mm)
## Micro-vessel Thickness

<table>
<thead>
<tr>
<th>Method</th>
<th>MV #1</th>
<th>MV #2</th>
<th>MV #3</th>
<th>MV #4</th>
<th>MV #5</th>
<th>MV #6</th>
<th>ALL (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Intensity Projection</td>
<td>769</td>
<td>562</td>
<td>1173</td>
<td>572</td>
<td>542</td>
<td>1136</td>
<td>792 ±293</td>
</tr>
<tr>
<td>Super-Localised MBs</td>
<td>227</td>
<td>172</td>
<td>151</td>
<td>157</td>
<td>153</td>
<td>126</td>
<td>164 ±34</td>
</tr>
<tr>
<td>Maximum Intensity Projection with Motion Correction</td>
<td>575</td>
<td>474</td>
<td>1015</td>
<td>520</td>
<td>520</td>
<td>1180</td>
<td>714 ±303</td>
</tr>
<tr>
<td>Super-Localised MBs with Motion Correction</td>
<td>115</td>
<td>91</td>
<td>90</td>
<td>80</td>
<td>108</td>
<td>87</td>
<td>95 ±13</td>
</tr>
</tbody>
</table>

\( \lambda = 250 \, \mu m \) (full bandwidth)  
\( \lambda = 500 \, \mu m \) (second harmonic)
Healthy Volunteer

Before Exercise

All MB events (number of counts) with Motion Correction

Total Events = 630k

After Exercise

All MB events (number of counts) with Motion Correction

Total Events = 990k
Healthy Volunteer

Before Exercise

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All MB events (number of counts) with Motion Correction

After Exercise

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All MB events (number of counts) with Motion Correction
Preliminary Results – Healthy Volunteer

- 4 healthy volunteers (V1, V2, V3, V4)
- 2 different days (A, B)
- 2 ultrasound scans to calculate relative change (baseline and after exercise)
- A total of 16 ultrasound scans

Summary

- In vivo super-localisation images were generated with a clinical scanner.
- Two-stage motion correction was performed:
  - Rigid Motion Correction (to reduce the large movements)
  - Non-rigid Motion Correction (movement reduction in the first stage creates a better starting point for the second stage, which eventually reduces the error)
- Future work will be on 3D imaging to compensate for out of plane motion.
- This technique has great potential when combined with motion correction.
  - Improvement in spatial resolution: ~5 times without motion correction
  - Improvement in spatial resolution: ~7 times with motion correction
- Super-Localisation achieves better delineation of microvasculature from larger vessels. Diffraction limited resolution may mask the details associated with PAD.