**Outline**

Page

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **1**  **2** | **Specific Aims**  **Human Health Significance** | | | | | 4  5 |
|  | 2.1 | | Etiology of stroke and the role of atherosclerotic plaque | | | 5 |
|  | 2.2 | | Clinical carotid ultrasound and plaque characterization | | | 5 |
|  |  | | 2.2.1 Defining vulnerable plaque | | | 5 |
|  |  | | 2.2.2 Plaque characterization with other methods and imaging modalities . . . . | | | 5 |
|  |  | | 2.2.3 Plaque characterization with diagnostic ultrasound | | | 5 |
|  | 2.3 | | High frequency ultrasound on carotid plaque | | | 5 |
|  | 2.4 | | Transcranial Doppler for monitoring microembolic events | | | 5 |
|  | 2.4 | | References | | | 5 |
| **3** | **Recursive Bayesian Regularization Applied to Ultrasound Strain Imaging** | | | | | 7 |
|  | 3.1 | | Improvement of strain image quality with regularization | | | 6 |
|  | 3.2 | | Prior efforts in regularization | | | 6 |
|  | 3.3 | | Recursive Bayesian regularization | | | 6 |
|  | 3.4 | | Measurements of the regulation effectiveness | | | 6 |
|  |  | | 3.4.1 Uniform strain simulations and phantoms | | | 6 |
|  |  | | 3.4.2 Circular inclusion simulation and phantoms | | | 6 |
|  |  | | 3.4.3 Optimal Strain Regularization Sigma (SRS) | | | 6 |
|  |  | | 3.4.4 Degenerate behavior from insufficient sampling | | | 6 |
|  |  | | 3.4.5 Addressing a carotid reverberation | | | 6 |
|  |  | | 3.4.6 Improvement of carotid strain images | | | 6 |
|  | 3.5 | | Properties and role in strain imaging | | | 6 |
|  | 3.6 | | Summary | | | 6 |
|  | 3.7 | | References | | | 6 |
| **4** | **Unbiased Subsample Displacement Interpolation** | | | | | 7 |
|  | 4.1 | | Previously explored methods for subsample tracking | | | 7 |
|  |  | | 4.1.1 Methods that use properties of cross-correlation | | | 7 |
|  |  | | 4.1.2 Parametric and non-parametric methods | | | 7 |
|  | 4.2 | | Numerical properties of 2D sinc interpolation | | | 7 |
|  |  | | 4.2.1 Behavior of optimization methods | | | 7 |
|  |  | | 4.2.2 Dependence on window and tolerance | | | 7 |
|  | 4.3 | | Comparison with parametric methods | | | 7 |
|  | 4.4 | | References | | | 7 |
| **5** | **Calculating Strain From Displacement** | | | | | 7 |
|  | 5.1 | | The strain tensor | | | 7 |
|  |  | | 5.1..1 Mechanical model | | | 7 |
|  |  | | 5.1.2 Acoustic model | | | 7 |
|  | 5.2 | | Methods for estimating strain from displacement | | | 7 |
|  |  | | 5.2.1 Finite difference based methods | | | 7 |
|  |  | | 5.2.2 The least squares strain estimator | | | 7 |
|  |  | | 5.2.3 B-spline fitting | | | 7 |
|  | 5.3 | | Combination of normal strains and shear strain into single strain index | 8 | | | |
|  |  | | 5.3.1 Maximum principal strain | 8 | | | |
|  |  | | 5.3.2 Maximum shear strain | 8 | | | |
|  |  | | 5.3.3 Total strain energy | 8 | | | |
|  |  | | 5.3.4 Distortional energy | 8 | | | |
|  | 5.4 | | Generating accumulated strain from a time series | 8 | | | |
|  |  | | 5.4.1 Dynamic frame skip | 8 | | | |
|  |  | | 5.4.2 Eulerian approach to accumulated strain | 8 | | | |
|  | 5.5 | | References | 8 | | | |
| **6** | **High-frequency Phantom Characterization** | | | 9 | | | |
|  | 6.1 | | Phantom design | 9 | | | |
|  | 6.2 | | Attenuation characterization | 9 | | | |
|  | 6.3 | | Phase velocity characterization | 9 | | | |
|  | 6.4 | | Absolute backscatter measurement | 9 | | | |
|  | 6.5 | | References | 9 | | | |
| **7** | **High-frequency Plaque Characterization** | | | 9 | | | |
|  | 7.1 | | Integrated Backscatter Calculation | 9 | | | |
|  | 7.2 | | Comparison with B-Mode | 9 | | | |
|  | 7.3 | | Comparison with Pathology | 9 | | | |
| **8** | **Transcranial Doppler Detection of Microemboli** | | | 10 | | | |
|  | 7.1 | | Methods to increase robustness of unstable data | 10 | | | |
|  |  | | 7.1.1 Examination room protocol | 10 | | | |
| **8** | ***In vivo* Quantification of Carotid Plaque Strain** | | | 10 | | | |
|  | 8.1 | | Strain estimation algorithm | 10 | | | |
|  |  | | 8.1.1 Hierarchical framework | 10 | | | |
|  |  | | 8.1.2 Reduction of peak-hopping in a hierarchical framework | 10 | | | |
|  | 8.2 | | Strain images | 8 | | | |
|  | 8.3 | | Cardiac cycle waveforms | 8 | | | |
|  | 8.4 | | Histological classification | 10 | | | |
|  | 8.5 | | Transcranial Doppler | 10 | | | |
|  | 8.6 | | Symptomatic/Asymptomatic status | 10 | | | |
|  | 8.7 | | MRI indices of neural atrophy and ischemia | 10 | | | |
|  | 8.8 | | Neuropsychological assessment | 10 | | | |
|  | 8.9 | | References | 10 | | | |
| **9** | | **Summary and Conclusions** | | | 12 | | |

|  |  |  |  |
| --- | --- | --- | --- |
|  | 8.1 | Histological classification | 11 |
|  |  | 8.1.1 Registration methods | 11 |
|  |  | 8.1.2 Strain imaging results | 11 |
|  |  | 8.1.3 Backscatter results | 11 |
|  | 8.2 | Transcranial Doppler | 11 |
|  | 8.3 | Symptomatic/Asymptomatic status | 11 |
|  | 8.4 | MRI indices of neural atrophy and ischemia | 11 |
|  | 8.5 | Neuropsychological assessment | 11 |
| **9** | **Summary and Conclusions** | | 12 |