COST Action CA16103
Magnetic Resonance Imaging Biomarkers for Chronic Kidney Disease (PARENCHIMA)

Minutes
Workung Group 2 Meeting, Koper, Slovenia
2020-03-03/04

Present: Amira Serifovic-Trbalic, Erlend Hodneland, Peter Rogelj, Feriel Romdhane, Julia Stabinska Frank Zöllner, Peter Rogelj
Remote participation: Rafael López González, (Antonio Pinheiro, Rebeca Echeverria Chasco)

Actions highlighted

Day 1:

- Presentation of status of the Database (Frank)
  - only one dataset available from Bergen (40 cases)
  - single test data in the system
- Presentation/ refresher on Using the Database (Raphael)

- Discussion on Improvements for the Database

  - for sharing data in the project it is important to have an idea what data is available
  - need a view that gives information on

  Result:
  - have the data uploaded into Quibim and compile list from there? (Quibim needs to add such functionality)
  - Allow general data sharing to registered members of the project through Quibim database (option during upload ?) -> ask Quibim
  - if not, make a google form from and have the content populated into the webpage (Frank -> ask Marcos) ?

- What information is needed to allow sharing of data?

Register for renal data (perspective of the user)

- Type of data: Pre-clinical or clinical or phantom*
- Purpose of the study / Type of pathology / healthy volunteers*
- Basic acquisition information
    - MR modality*
    - Field strength, vendor
    - Data dimension (2D, 3D, 4D, ...)
    - resolution
- Number of cases*
- Reference values (segmentations, kidney parameters (eGFR etc), …)
- Link to publication if available*
- Contact detail of the data supplier*
- Advanced acquisition information
    - motion compensation
    - type of sequence / variants
    -
- Sharing limitations*
- Data format available*

*main information

- Further actions:
    - Ask Quibim to alter the system including the information above. (-> checked with Quibim, Raphael)
    - Ask Quibim by default share the data to all users in the Parenchima (-> checked with Quibim, Raphael)
    - If 1 and 2 are not feasible, go for the google form (needs to be moderated by someone?)
    - Use WG3 list of renal studies to approach people to submit data to the database (Frank -> distribute list + template letter, all: approach people)

Day 2:

- Evaluation of renal registration

Talks were given by Frank Zöllner, Amira Serifovic-Trbalic, Erlend Hodneland, Peter Rogelj and Feriel Romdhane. Following are some summaries provided by the authors.

Amira Šerifović-Trbalić, University of Tuzla, Bosnia and Hercegovina
The presentation held by prof. Amira Šerifović Trbalić is an overview of the MR image registration evaluation principles currently used. Prior to a clinical application, the medical image registration algorithms for renal MRI need to be carefully validated. Validation of registration accuracy, especially for non-rigid image registration methods, is considered as a non-trivial and difficult task, because the ground truth (i.e., gold standard) is generally not available.
The image registration algorithms are aimed towards solving multiple problems that arise during renal image alignment, such as: rich variety in the anatomy and pathology; lack of fiducial markers on the kidneys; change in the intensity in a

MR image during data acquisition; variability in kidney motion and geometry in MRI images, and the lack of standard data sets. Evaluation of registration approaches often relies on: the visual inspection by an expert user, the quantification based on manually or automatically identified anatomical landmarks or based on manual registration/segmentation, a controlled study using computer simulations or physical phantoms. Although significant work has been done in the field of renal image registration, there is much room for the development of validation strategies.
Due to missing agreement on a registration quality measurement, it is difficult to make a quantitative comparison between registration algorithms.
For the details see https://link.springer.com/article/10.1007%2Fs10334-019-00782-y.

Frank Zöllner, Heidelberg University, Germany
- Several difficulties regarding evaluation of image registration may be avoided using phantoms and synthetic data (synthetic images or synthetic deformations).

Erlend Hodneland, NORCE, Bergen, Norway
Presentation key points:
- Geometric model that incorporates poroelasticity (instead of elasticity only) improves registration results.
- Image registration can only moderately well restore the true deformation field. Although images may indeed get visually correctly matched, deformation is not correct.
Visual overlap and deformation correctness are not necessarily correlated – geometrically better results may look worse.
- MRI biomarkers are not considerably affected by incorrect deformations inside compartment regions.
- Image post processing (e.g., registration) has lower influence on biomarkers than selection of appropriate image acquisition parameters.

Peter Rogelj, University of Primorska, Koper, Slovenia:
Evaluation of image registration methods based on segmented points
We present our solution for evaluation of image registration implemented as a part of the REG-toolbox, a medical image registration toolbox for Matlab and Octave, which is available for free on Github: https://github.com/progelj/REG-toolbox. There are simple graphical interfaces available for segmenting feature points, defining ROI masks and visual inspection of registration results. There are also functions to evaluate registration results by measuring standard deviations of point positions. The difficulty of this evaluation approach is in the need for manual feature point segmentation that requires involvement of experts and is subjected to interobserver variability.

Feriel Romdhane, Molecular Biotechnology Center (MBC), University of Turin, Italy:
CEST and DCE MRI data at preclinical level
Chemical exchange saturation transfer (CEST) imaging is a novel MRI-based contrast technique that has potential to provide molecular information for diagnosing pathological tissues and the detection of molecular responses to treatment. The basic principle of CEST is that the exchangeable protons in specific molecules (in our case iopamidol) are selectively saturated by successive RF (Radio frequency); the saturation is transferred upon chemical exchange to the bulk water pool with decreasing in MRI signal of the water; As a result, contrast is thus generated by imaging the signal difference of protons in bulk water.
In general, CEST also suffers from the same problems as in MRI, Subject motion is especially problematic in CEST data analysis as it relies on

comparison of images acquired at multiple offset frequencies. The acquisition of multiple CEST images results in long scan times when using traditional imaging readouts. This long scan time causes CEST MRI to be affected by motion introducing field inhomogeneity, shifting offset frequencies and causing distortions in CEST spectra that resemble true CEST effects.
The effect of motion in CEST MRI is almost unexplored and few studies examine motion correction in CEST MRI with some limitations. Therefore, developing a correction approaches to improve the CEST MRI acquisition is essential and encouraging.

- Discussions:

  Three evaluation methods have been identified. We have also identified their advantages (+) and limitations (-):
  1. Evaluation based on control points:
  + simple implementation of the evaluation when ground truth is available
  + only three control points needed for evaluation of rigid registration algorithms
  + evident meaning of the results provided in millimeters
  - difficult to obtain ground truth data (segmentation protocol and experts required, motivation needed to attract the experts)
  - inter-observer variability (multiple observers needed)
  The method and all the required tools are already implemented in Matlab/Octave by REG-toolbox (https://github.com/progelj/REG-toolbox)
  2. Evaluation based on segmented regions:
  - segmentation needed, more time consuming than segmentation of a few control points
  + segmented regions provide volumetric information
  - 3D effect affect the evaluation due to normally larger inter-slice distances.
  - evaluation of the boundary error only
  - results are more difficult to interpret: overlap index (Dice similarity coefficient) is not provided in distance units (mm), Hausdorff distance provides only the maximal error.
  3. Voxel intensity curves
  + commonly used in for renal registration evaluation
  - a numeric evaluation requires method extensions (estimation of curve smoothness for every voxel and statistical analysis, e.g. cluster analysis)
  Visual evaluation techniques are not appropriate as they do not provide numeric results that could be compared for different methods.
  The identified evaluation methods can be supplemented by additional measures of deformation/ displacement fields (temporal periodicity, amplitude, volume change).

- Selection of data for renal image evaluation:

  At the moment the only data available for the evaluation present in the Quibim database is the one provided by Eli Bjøvad Eikefjord.

  There were some assumptions expressed that segmentations (whole kidney and compartments) may also be available for that data. In addition to this reference GFR data is available and eventually some registration results.

  For segmentation of feature points some student may be engaged, but it is not likely to be able to get one. Consequently, the data can be evaluated only using methods 2 and 3.

  The group from Torino offered a preclinical data (mice) that could be freely shared. The group can also offer some segmentations (segmented feature points and regions).

Further agreements and selection of evaluation methods will be made after the meeting.

- Further actions:
  - Feriel and Peter analize possibilities for evaluation based on the preclinical data.