AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND NEW ZEALAND

Integrating spine biomechanics with ^{18}F-NaF PET/CT imaging to assess lumbar pain and bone remodelling

Master's Thesis by Andi Shen Liu, supervised by Dr Justin Fernandez, Dr Jacob Munro, and Dr Vickie Shim

Background

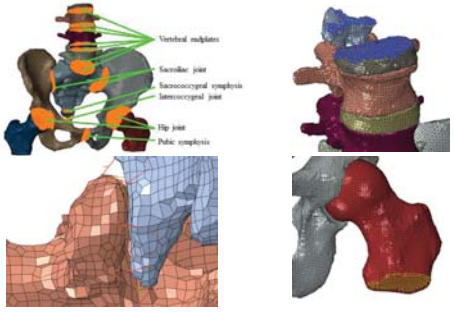
^{18}F-fluoride as a sodium salt (^{18}F-NaF) is a radiotracer used in PET imaging, and has only recently been used to evaluate back pain [1]. For this purpose, in children and young adults a combined PET/CT is often used [2]. Their ^{18}F-PET images show abnormal focal uptake at an earlier stage of stress (fatigue) fracture than visibility of fracture in the CT image [2].

Previous studies demonstrate a link between increased ^{18}F uptake, bone remodelling as a result of abnormal stress or fracture, and pain. None compare the location and magnitude of stress distributions in the lower spine with that of ^{18}F uptake.

For this thesis historical data sets consisting of pairs of ^{18}F-NaF PET and CT scans of the lumbar region of 29 patients were provided. The images had been acquired following self-reported chronic lumbar pain.

Workflow

1. Image segmentation of 29 patients' vertebrae from CT, and of Visible Human Male vertebrae, intervertebral discs, hip, femurs
2. Meshing of VHM parts and finite element model assembly
3. Extraction of node vertices from VHM Abaqus INP file to CMISS IPDATA format → Host-mesh customisation of VHM mesh node coordinates to patients' CT meshes → Subject-customisation of the VHM Abaqus INP file using the subject-customised coordinates and subject-specific body weights
4. Abaqus simulations and export of Von Mises Stress at element centroids as IPDATA file → Interpolation of ^{18}F from each patients' PET image to these element centroids
5. Colocalisation analysis



Above: Details of the Abaqus finite element model. Clockwise from top left: tied surfaces, fixed nodes, load applied at femur surface, connector elements.

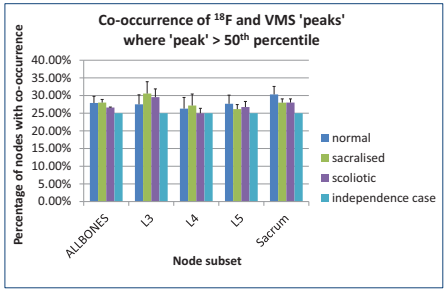
Colocalisation Analysis

Colocalisation of two fields can be thought of as consisting of **co-occurrence** (spatial overlap), and **correlation** (co-distribution in proportion to one another).

Correlation tests on a per-node basis at the element centroids showed no significant correlation between the magnitude of ^{18}F and Von Mises Stress.

Two measures of co-occurrence were tested:

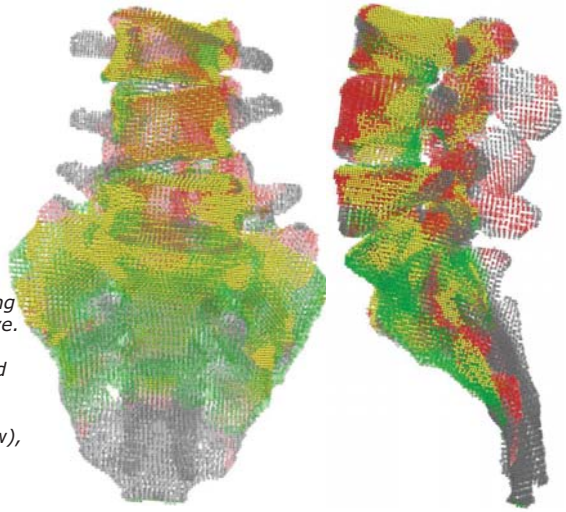
1. ***P*('*peak ^{18}F*' ∩ '*peak VMS*' | '*peak VMS*') – nodes with co-occurrence as a proportion of all 'peak VMS' nodes** using 'peak' thresholds defined **manually**.
   Results:
   Some patients showed high co-occurrence (80%), but there was no general case from independence of distribution of the two fields to compare different patients against.
   T-tests using BMI, gender, and age as grouping factors did not show these factors in isolation to cause significant differences between the co-occurrence in each group.
2. ***P*('*peak ^{18}F*' ∩ '*peak VMS*') – nodes with co-occurrence as a proportion of all nodes in certain node subsets** using 'peak' thresholds defined by **quantile** intervals.
   This allows a pre-defined proportion of 'peak' nodes to be specified.
   The expected co-occurrence for an independently-distributed general case can now be calculated by *P*('*peak ^{18}F*') × *P*('*peak VMS*').
   This independent distribution case was used as a comparison to which the mean and standard deviation of patient groups 'normal', 'sacralised' (possessing a lumbosacral transition vertebrae fused to the top segment of the sacrum) or 'scoliotic' (bend in the coronal plane) could be compared.
   See graph below for the results from defining peaks in the percentile interval 50th-100th.



*Above: Group mean and standard deviation using co-occurrence measure **2** described in text above.*

*Right: Using the 50th percentile as the threshold value as described in co-occurrence measure **2**, nodes in a scoliotic patient with*

- *co-occurring 'peak ^{18}F' and 'peak VMS' (yellow),*
- *'peak ^{18}F' without 'peak VMS' (green),*
- *'peak VMS' without 'peak ^{18}F' (red),*
- *neither 'peak VMS' nor 'peak 18F' (grey).*



Summary

^{18}F-NaF PET/CT scans of 29 patients with lumbar pain were provided. Von Mises Stress at element centroids from subject-customised finite element simulations were derived from the CT scans, and ^{18}F uptake was interpolated from the PET scans to these centroids.

On a per-node basis, no correlation was found between ^{18}F and VMS magnitude.

However, co-occurrence between 'peak' ^{18}F and VMS higher than that expected for an independent-distribution case was found when 'peaks' were defined using the 50th-100th percentile interval.

Refer to my thesis for details of the results from using other intervals, and for further details and discussion. The appendices include self-written code to solve problems such as automatic sizing of the host mesh, and fitting of intervertebral discs using nodes on surrounding vertebrae.

References

1. Lim, R., et al., *Early experience with fluorine-18 sodium fluoride bone PET in young patients with back pain.* Journal of Pediatric Orthopaedics, 2007. **27**(3): p. 277-282.
2. Grant, F.D., *^{18}F-Fluoride PET and PET/CT in Children and Young Adults.* PET clinics, 2014. **9**(3): p. 287-297.

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