ATLAS-BASED CORRELATION OF LOCAL TRABECULAR DIRECTIONALITY AND DEFORMATION WITH SERUM MARKERS OF BONE TURNOVER IN LUNG TRANSPLANT RECIPIENTS IN A LONGITUDINAL SETTING

L. Fischer[1,5], A. Valentintisch[1], T. Gross[4], D. Kienzl[2], C. Schueller-Weidekamm[3], F. Kainberger[1,3], J. Patsch[1,3], G. Langs[1], M. D. DiFranco[1,6]

(1) CIR Lab, Dept. of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna (2) Division of General and Paediatric Radiology, Dept. of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, (3) Dept. of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna (4) Institute of Lightweight Design and Structural Biomechanics, Vienna University of Technology (5) Christian Doppler Laboratory for Ophthalmic Image Analysis, Dept. of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna (6) Quantitative Hybrid Imaging Lab, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna

MEDICAL UNIVERSITY OF VIENNA

CIR

Purpose

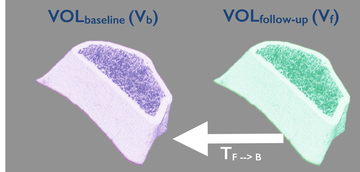
Non-invasive assessment of changes in bone microarchitecture over time can be performed by high-resolution peripheral quantitative computed tomography (HRpQCT). The aims of this pilot study were to develop a methodology for the quantification of trabecular reorganization beyond standard morphometry and to investigate the relation between trabecular reorganization, bone strength as captured by finite element analysis, and serum markers of bone turnover.

HRpQCT baseline and follow-up scans of the distal radius from lung transplant (LuTX) patients were obtained (n=33, 15±5 month mean interval). Serum markers (CTX, OCN) were captured at each time point. Finite element analysis (FEA) was employed to measure stiffness (k), failure force (Fmax), bone strength (σmax). Manufacturer-provided standard bone morphology parameters were also acquired.

Baseline and follow-up scans were rigidly registered and deformation maps were obtained for each case[1]. Three parameters related to local changes in trabecular orientation and the direction of deformation were obtained: entropy of directionality (**ED**), entropy of Jacobian (**EJ**), and symmetric Kullback-Leibler divergence (**KLD**). All derived parameters were then correlated to the serum, FEA and morphology values on 3D grid-based regions of an atlas generated from the entire study population.

Methodology

REGISTRATION
Follow-up to Baseline Volume



V_b and V_f represent HRpQCT volumes normalized to BMD values. Volume registration is performed in 2 steps:

(1) Alignment of cortical surfaces
(2) Trabecular compartment registration

The resulting transformation ($T_{F \dashrightarrow B}$) is then applied to V_f, and order 3 b-spline interpolation is applied in to obtain a registered volume V_f'. Finally, V_b is normalized with a Gaussian filter in order to obtain V_b'. This is done because of the interpolation required in generating V_f'.

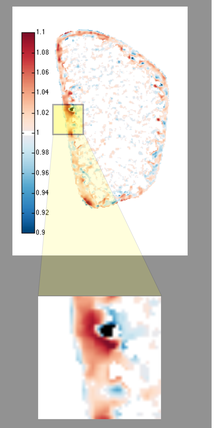
LOCAL VOLUME CHANGE
Jacobian Determinant from Optical Flow

Optical Flow calculates a 3-D vector at each voxel in the registered volume (V_f'). This vector describes the direction and magnitude of the change in image intensity at that voxel relative to V_b'.

The **Jacobian Determinant (J_V)** is a scalar measure derived from the optical flow vector field which describes local volume change at each voxel in the following way:

- $J_V > 1$: local growth
- $J_V < 1$: local shrinkage
- $J_V = 1$: no change

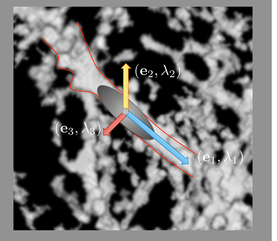
The value of J_V at each voxel creates a deformation map between V_b' and V_f'.



LOCAL TRABECULAR DIRECTIONALITY
Structure tensors

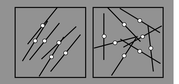
Trabecular directionality **D** is obtained by computing **structure tensors** based on a vesselness diffusion filter [2].

The directions are derived by performing an eigenvalue decomposition of the Hessian matrix of V_b and V_f. Elongated tubular structures are described by eigenvectors with the smallest eigenvalue.

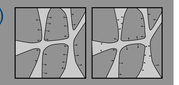


ADVANCED MEASURES OF MORPHOMETRY
Entropy and Kullback-Leibler Divergence

Entropy of trabecular orientation (**ED**) captures the distribution homogeneity of orientations of trabeculae.

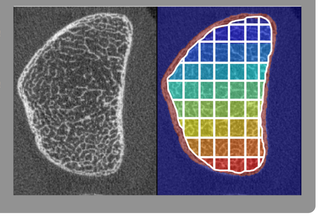


Entropy of trabecular volume change (**EJ**) captures the distribution homogeneity of trabecular volume change.

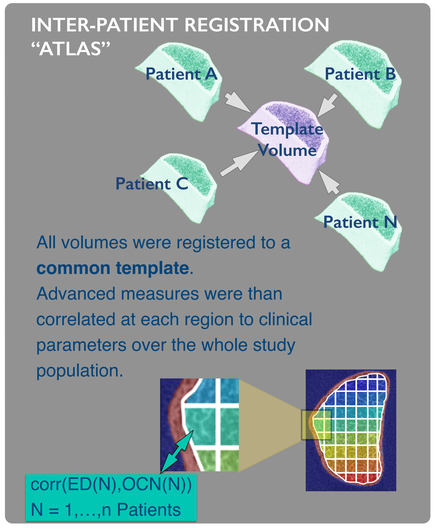


Kullback-Leibler divergence of direction and volume change (**KLD**) captures the relationship among dominant trabecular orientation and volume change.

All three measures are computed in block-like regions over the whole scan volume height.



Methodology cont.



Results and Examples

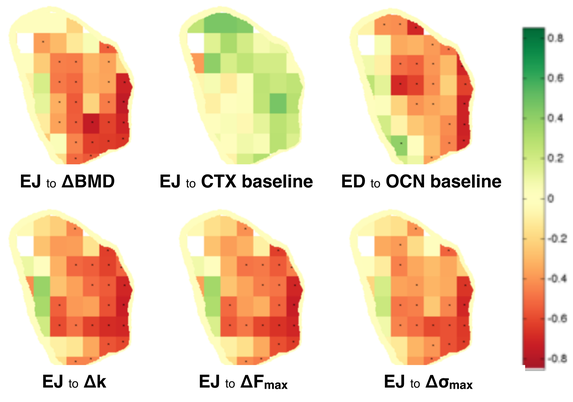


Figure 1: Regional maps of atlas-based correlations between derived measures of local trabecular changes and serum markers, BMD and finite element analysis parameters. A star represents statistical significance ($p < 0.05$). Each map is based on the middle slice of the HRpQCT atlas volume (9mm depth), and each grid region represents a 3D volume. White signifies too little information for a correlation.

- Significant ($p<0.05$) localized negative correlations between **EJ** and changes in **BMD**, **k**, F_{max} and σ_{max} were seen.
- **OCN** at baseline showed significant localized negative correlations with **ED**.
- **CTX** at baseline showed localized positive correlations with **EJ**, but not to the level of significance.
- The **OCN** to **ED** negative correlation suggest that within the LuTX cohort, region-specific dominant trabecular directionality is observed where **OCN**, a formation marker, is elevated.
- A positive **CTX** to **EJ** correlation could indicate that direction-independent bone loss is observed in conjunction with elevated CTX, a resorption marker.

Conclusion

We have proposed a methodology for discovering localized correlations between image-derived measures of trabecular reorganization and various bone metabolism, biomechanical and morphology markers.

Application of this method to a LuTX cohort reveals correlations between trabecular directionality and both local systematic bone turnover and bone strength.

References

[1] DiFranco M. ASBMR 2013/SA0072
[2] Manniesing R, Viergever MA, Niessen WJ. Vessel enhancing diffusion: a scale space representation of vessel structures. Medical Image Analysis2006; 10(6): 815–825.

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matthew.difranco@meduniwien.ac.at www.cir.meduniwien.ac.at