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AAO Foundation Final Report Form
(a/o 1/3/2018)

Type of Award: Biomedical Research Award

Name(s) of Principal Investigator(s): Lucia Cevidanes

Institution: University of Michigan

Title of Project: Integrative Predictors of Temporomandibular Joint Osteoarthritis

Period of AAOF Support: 07-01-18 to 12-31-19

Amount of Funding: $30,000

Summary/Abstract

In this BRA, we scaled up our systematic phenotyping of TMJ OA through the Data Storage Computation and Integration (DSCI) web-based system. This web-based system decentralizes powerful algorithms in a deep learning neural network that integrates imaging, clinical and biological markers, using a multivariate varying coefficient model of high dimensional data relationships to condylar morphology.

Web-based Development: We have developed the Data Storage for Computation and Integration, DSCI, system to manage and analyze the clinical, biological and imaging data. During Year 6, we developed a new graphical user interface to upload and share files on the web platform, currently in beta-testing stage. The updated front-end of DCSI is based on HTML components using REACT. The clusterpost plug-in allows submitting tasks to remote computing grids and access to use of the data stored in the system. Prior to testing with collaborative centers, security and privacy of the access to DSCI is handled using JSON Web Tokens (JWT), with JWT encryption of each authorized user login. The web Data Management server architecture facilitates scalability and inclusion of plugins or processing pipelines to exploit data sets stored in the web system. The web system architecture uses the Javascript engine Node, to orchestrate between different components of the web system:

- Uses Hapi, as the server framework, to build services focusing on writing reusable application logic.
- A NoSQL type database, Couchdb, to store data sets in a collection of independent JSON documents. The JSON flexible format facilitates encoding data without enforcing a predefined rigid structure.
- The relationships between data stored in the system is discovered using the MapReduce algorithm, and creates indexed views of unique patient anonymized ids.

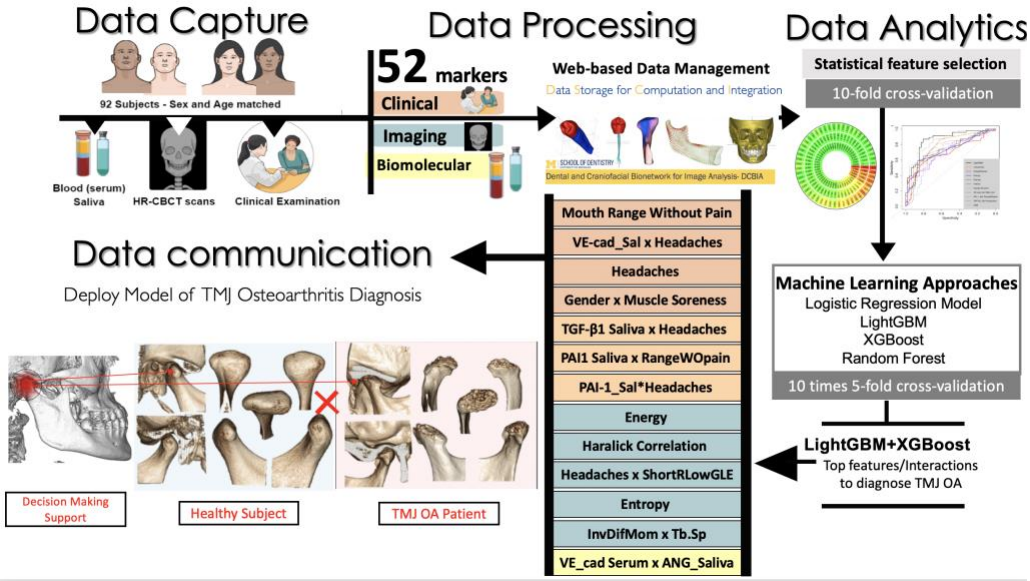

Figure 1. Results reported by Bianchi et al, Scientific reports, under review

Neural network structures: We have packaged the scripts for statistical analysis and machine learning-based prediction methods XGBoost and LightGBM, available at Github, https://github.com/tli3/OAI**.** We have tested preliminary integrated biomarkers/features: Clinical, Trabecular (Radiomic), Biomolecular (Saliva and Serum). The outputs are Statistical association analysis, Manhattan plots (p values, q values, AUC), Circle plots (p-values, q-values, AU), Prediction results: XGBoost, LightGBM, Ensemble. We implemented cross-validation approaches (10 times 5-fold Cross Validation) with ability to compute AUC, ACC, F1-Score, Precision, Recall, Plots of ROC curve, Mean Importance Scores, Boxplot of importance scores for top features selected, Two sample boxplot for comparison of top features among OA vs Normal group; p-values reported from Mann–Whitney U test. All tests were performed with available training datasets (Figure 1).

Patient Specific Classification and Prediction (PSCP) tool development: The data analytics of shape features requires generating 3D models of the condyles improve shape correspondence, and extracting features from the 3D models, which is already implemented to our previous ShapeVariationAnalyzer prototype, now called PSCP tool. The shape features extracted at each of the 1002 vertices of the condylar meshes include normals, curvatures, distance to mean groups, and heat kernel signature. These purely geometric features are proposed because they led to higher accuracy in classification in our preliminary studies, and do not depend on the position nor the orientation of the model, which may vary across the different groups in the population. A consensus visualization and consensus interpretation of high resolution CBCT multi-planar slices by two expert radiologists (Dr. Benavides and Soki) was used to classify subjects with clinical diagnosis of TMJ OA (paper in preparation Bianchi et al, Radiographic Diagnosis of TMJ Degenerative Joint Disease: false positives or asymptomatic

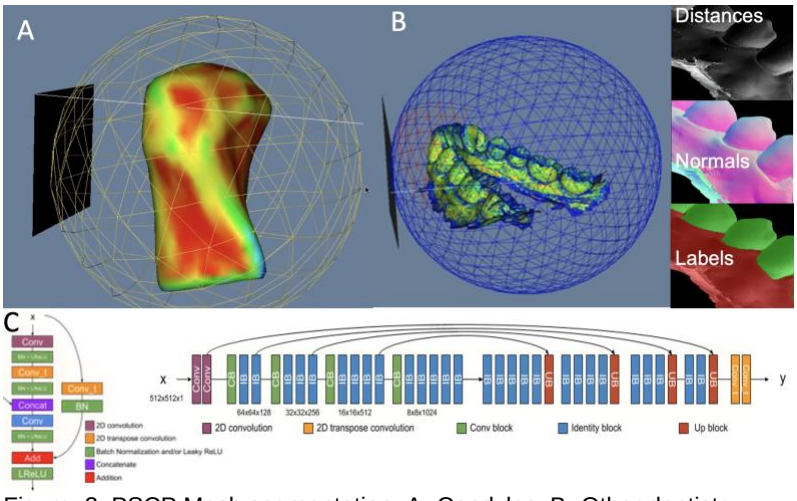

Figure. 2. PSCP Mesh segmentation. A- Condyles; B- Other dentistry applications; C- Up block+ RUNET neural network architecture being tested.

degeneration). The radiologists classified the condylar morphology into different degrees of condylar degeneration that will later be compared to the PSCP automatic classification. The PSCP neural network has tested the segmentation of the region of interest with a sphere around it and a plane tangent to the surface of the sphere. The sphere helps locate and position the planes that will acquire or probe the surface of the object using a ray cast approach to enable powerful deep learning-based techniques with state-of-the- art performance (Figure 2).

Maintenance of methods and algorithms in open-source SlicerCMF: We have provided maintenance and support for each module in SlicerCMF disseminated in a separate Github repository as part of the DCBIA organization. Improvements introduced:

- We changed the Python based modules to be compatible with Python 3. This was the most urgent task since the recent versions of Slicer are packaged with Python 3. Also, Python 2.7 is no longer maintained past 2020. Thanks to this work, most of our modules compile with the current Slicer nightly.
- The heads of the repositories were pointed to each individual developer and we changed the inheritance tree in the github repository to make sure the main repositories were in the DCBIA organization.
- We added a 3d-slicer-extension topic to each code repository to support lookup of Slicer extension source code using the GitHub website or associated developer API.
- Dashboard reports associated with each SlicerCMF extension have been reviewed, then build and testing errors have been reported in the corresponding issue trackers. For existing extensions that could be successfully built, issues like incorrect results and UI inconsistencies have also been reported.
- Collection of input datasets and expected outputs for each SlicerCMF module, that can be found here.

The work related to Aim 1 goals on learning approaches to integrate quantitative markers for diagnosis and assessment of progression of TMJ OA, as well as extending capabilities of 3D Slicer4 into web-based tools and dissemination of open source image analysis tools, have led to 18 papers already available in pubmed, 6 accepted papers and 4 other papers under review since 2019.

Response to the following questions:

1. Were the original, specific aims of the proposal realized? Yes
2. Were the results published?
    a. References:

1. Shoukri B, Prieto JC, Ruellas A, Yatabe M, Sugai J, Styner M, Zhu H, Huang C, Paniagua B, Aronovich S, Ashman L, Benavides E, de Dumast P, Ribera NT, Mirabel C, Michoud L, Allohaibi Z, Ioshida M, Bittencourt L, Fattori L, Gomes LR, Cevidanes L. Minimally Invasive Approach for Diagnosing TMJ Osteoarthritis. J Dent Res. 2019 Sep;98(10):1103-1111. doi: 10.1177/0022034519865187.
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b. Was AAOF support acknowledged? Yes
c. If not, are there plans to publish? N/A

3. Have the results of this proposal been presented?
    a. If so, list titles, author or co-authors of these presentation/s, year and locations

Abstract presentations:

1. Cevidanes L. 3D Craniofacial Image Registration in Dentistry for Assessment of Treatment Response. J Dent Res 2019; 98 (Spec Iss B):0014
2. Shoukri B, Aronovich S, Sugai J, Cevidanes L, Ruellas A, Yatabe M, Benavides E, Prieto JC, Paniagua B, Ashman L, Styner M, Zhu H. Biomarkers and Neural Network Approach in Predicting Temporomandibular Joint Osteoarthritis. J Dent Res 2019; 98 (Spec Iss B): 2299.
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Professional development workshops:

TMJ anatomy, pathologies, imaging and therapies Workshop, Poland, May 2019
Kokich-Shapiro Lecturer, Seattle May 2019
Quantitative morphology - a workshop on the analysis of 3D imaging data, during International

Association of Dental Research June 2019
3D Imaging Workshop, University of Fortaleza, Ceará, Brazil, Outubro 2019

Professional development presentations:
SPIE International Society of Optical Engineering, Medical Imaging, Feb 2019
American Association of Anatomy, Experimental Biology meeting, Orlando, March 2019
American Association of Orthodontics, Los Angeles, May 2019
International Association for Dental Research, Vancouver, Canada, June 2019

b. Was AAOF support acknowledged? Yes

4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

AAOF funding has been instrumental for preliminary data towards and NIH R01024450 on Integrative Predictors of Temporomandibular Joint Osteoarthritis