OVERVIEW: Cone beam CT (CBCT) is frequently used in dental practice for various applications such as endodontics, orthodontics, prosthodontics, and surgical implant treatment planning. Certain incidental findings present in scans may go unnoticed by dentists with limited familiarity of head and neck soft tissue anatomy[1]. Vascular calcifications are potentially significant incidental findings that are associated with several comorbidities such as diabetes mellitus, renal disease, cardiovascular disease (CVD) and risk of cerebrovascular incidents[2-4]. With growing number of CBCTs, dental providers may be the first to encounter these biomarkers in otherwise healthy asymptomatic patients and make proper referral as a preventative measure. Failure to detect these calcifications may result in delayed medical care and poor prognosis. Manual identification of these calcifications by dental providers is not only time-consuming but can also be challenging due to proximity to other structures with similar attenuation such as bone, or similarity in appearance to other entities such as tonsillar or dural calcifications, or artifacts. There is thus a strong unmet clinical need for accurate segmentation and characterization of vascular calcifications.

Proposed Approach and Clinical Significance: We propose a two-stage approach. First, we will develop a robust automated calcification detection and segmentation framework that can be trained with limited imaging datasets. Second, we propose to extract computational imaging features from the identified calcification regions and study their prognostic relevance, i.e., their ability to predict CVD. Developing an automated system for detection and localization of carotid artery calcifications can: **1)** Help identify patients with this significant incidental findings, and **2)** Reduce time to detect the finding. As a result, dentists can make the proper referral to physicians and improve patient care. Further, characterizing the morphometry and texture of these calcifications and studying their association with CVD can help establish computational risk factors for prediction of the various manifestations of CVD. Currently, there are no established quantifiable metrics for prediction of CVD based on the severity and extent of vascular calcifications from CBCT data. Having a quantifiable metric can significantly assist the clinician with an objective risk assessment that can lead to proper patient management. We plan to accrue data from N=1000 patients.

Innovation: **1)** A major challenge in dental image segmentation is availability of high quality and large volume of training datasets. Additionally, the segmentation target in our case is extremely small (less than 1% of the entire image volume - See **Fig 2, 5**), rendering traditional approaches unsuccessful. Unlike traditional deep learning (DL) segmentation approaches that rely on vast amounts of training data and where the segmentation target is not small, we propose to develop a framework that leverages a self-pretraining paradigm to reliably and robustly segment the calcifications even when training data is limited and the target region substantially small. **2)** Though vascular calcifications have been shown to be associated with risk of CVD, the imaging presentation of these calcified regions in CBCT is relatively understudied. We hypothesize that the morphometry and textural features from these regions have significant prognostic value and propose to study these using radiomic analysis. Leveraging cutting edge computational approaches, we will be the first to study CBCT extracted computational imaging biomarkers (CIBs) in addition to traditionally investigated clinical risk factors to strengthen our models' predictive capabilities. **3)** Another major innovation will be the development of an automated quality check and image standardization pipeline to address the challenges associated with varying image quality across scanners (See **Fig. 5**). Our effort will be the first of its kind in dental imaging and will benefit both clinicians and machine learning researchers.

The team has received favorable feedback (Impact Score: 45) from the NIH on the A0 proposal submission to the NIH National Institute of Dental and Craniofacial Research (NIDCR) R03 mechanism. The NIH Summary Statement acknowledged several positive aspects of the proposal, including the clinical significance of the identified problem, the notable expertise and capabilities of the team, as well as the innovative nature of the proposed project. To address these reviewer concerns (summarized in the Impact Statement), the OVPR seed funding will provide us with the requisite support and resources to undertake additional experimentation and research activities. These efforts are essential to bolster the proposal and enhance its overall quality. Consequently, we aim to re-submit a more robust and refined A1 proposal, either in the upcoming year or during the early months of 2025.