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Application of machine learning technologies for detection of proximal lesions in intraoral digital images: in vitro study.

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APPLICATION OF MACHINE LEARNING TECHNOLOGIES FOR DETECTION OF PROXIMAL LESIONS IN INTRAORAL DIGITAL IMAGES: IN VITRO STUDY

By

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B.D.S., Dr. NTR University of Health Sciences, 2017

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A Thesis Approved on

July 31, 2020

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DEDICATION

This thesis is dedicated to

My parents - Ravi Shankar and Roja Mani,

My sister - Ruta Rasagnya.

Tejaswi Nekkanti

Without their support, I would not have been able to complete the research.

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ABSTRACT

APPLICATION OF MACHINE LEARNING TECHNOLOGIES FOR DETECTION OF PROXIMAL LESIONS IN INTRAORAL DIGITAL IMAGES: IN VITRO STUDY

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Background: Interpretation of bitewing radiographs is influenced by factors such as acquisition parameters (e.g. exposure, type of sensor), clinical technique, visualization (e.g. monitor type and calibration) and the observer (e.g. experience and fatigue bias). We hypothesized that the use of artificial intelligence (AI) will reduce visualization and observer factor in bitewing interpretation and improve diagnostic accuracy.

Objective: The purpose of the present study was to evaluate the use of AI in the form of a machine-learning algorithm to detect and quantify proximal lesions compared with human trained observers.

Methods: 16,000 anonymized, digital bitewings of patients were hand searched and non-bitewing, poor quality images with personal health identifiers were excluded from the study. The images were randomly assigned into four sets: a) Training dataset for training AI, b) Calibration dataset for training 3 experts and 3 evaluators with AI software interface use, c) Ground truth set displayed to 3 experts used to provide a consensus truth, and d)

Testing Subset displayed to three general dental practitioners (GDP) and used to evaluate the performance of the AI and GDPs compared to the experts. Sensitivity and specificity were calculated and receiver operator characteristic analysis was used to determine accuracy and compared using ANOVA ($p \leq 0.025$).

Results: Overall sensitivity for AI (0.62) was greater compared to observers (mean, 0.52; range, 0.33-0.74) whereas specificity for AI (0.71) was reduced compared to observers (mean, 0.94; range, 0.87-0.98). Overall ROC for AI (0.7; CI: 0.66-0.74) was similar to the observers (0.74; CI: 0.69-0.78). Sensitivity increased for observers overall with increasing lesion (0.22 to 0.75) size but remained steady for AI (0.40 to 0.58)

Conclusion: Using a limited learning dataset, AI provided a higher sensitivity for proximal lesion detection and greater accuracy for incipient sized lesions than observers. Further AI training is necessary to increase the specificity of dental proximal lesion detection.

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CHAPTER I

INTRODUCTION

Dental caries is defined as the localized destruction of susceptible dental hard tissues by acidic by-products from bacterial fermentation of dietary carbohydrates.(1) Individuals are prone to dental caries at all stages of life. The National Institute of Dental and Craniofacial Research reports that in the United States 91% of adults aged 20 to 64 years had exposure to caries in some form, increasing to 96% for those aged 65 years and above.(2, 3) When timely intervention is not provided, dental caries may progress to the dental pulp causing agonizing pain and can ultimately result in tooth loss. Thus, reducing the impact of caries on an individuals' general health, quality of life, and financial burden is a significant public issue.

Clinical detection of dental caries on the proximal surfaces of adjacent teeth, either visually or through a dental explorer (tactile inspection), is especially challenging. Bitewing radiography (BWR) is generally the imaging technique of choice used to complement clinical evaluation of proximal surfaces. BWR has an average sensitivity of 50% and a specificity of 87% for detecting interproximal dental caries.(4) Clinicians can identify just about half of the dental carious lesions present using standard clinical and radiographic methods, and can misclassify sound surfaces as decayed.(1) In addition, the accuracy of human observers in detecting proximal dental caries on bitewing radiographs is influenced by various factors including the monitor,(5) the viewing conditions,(6-9) and the observer.(10)

Radiographic changes in the integrity of proximal surfaces of the crowns of the dentition occurs as a result of a reduction in the mineral content of initially the enamel and subsequently the dentin resulting in a net reduction in attenuation as the x-ray beam passes through the teeth.(11) The subsequent increase in radiographic density is recorded on an image receptor as a relative radiolucency and is referred to generically as a proximal lesion. Proximal surface demineralization can occur as a result of microbiological attack from the bacteria present in the oral cavity (dental caries) or dietary acid consumption through ingestion (i.e. food or drink) and regurgitation resulting in erosion.(12-14)

In recent years, advances in artificial intelligence (AI) have created computer-aided diagnosis (CAD) systems that provide assistance in decision-making to medical radiologists in such tasks as the detection of breast cancers in mammograms, detection and classification of diabetic retinopathy, skin cancer detection, and brain lesion localization.(15-18) The application of AI techniques in Dentistry have been reported for the detection of cephalometric landmarks, segmentation, and classification and detection of tooth and adjacent structures.(19-25)

The current study evaluates the use of AI in the form of a machine-learning algorithm to detect and quantify proximal dental caries compared with trained human observers. We hypothesize that the use of a machine-learning program reduces operator and viewing condition biases and will lead to increased accuracy and precision in the detection and diagnosis of proximal dental caries.

CHAPTER II

MATERIALS AND METHODS

Machine Learning Software

Denti.AI Technology Inc., (Toronto, ON, Canada) has developed a machine learning system to recognize and identify patterns of proximal dental caries on digital bitewing images. The software is web-based and automatically identifies potential dental carious lesions on proximal surfaces by using proprietary algorithms based on derived mathematical functions ("Models") used iteratively (over and over again) on a global set of images based on input from an annotated test or training data set. The Models analyze multiple images to derive mathematical representations of the digital patterns, referred to as *attributes*, associated with proximal dental caries. The purpose of the application of the software is to identify and recognize any attributes present on the digital radiographic image.

The Models are optimized using a combination of multiple proprietary algorithms. The algorithms incorporated contain certain significant novel technologies developed by Denti.AI Technology Inc., based on recurrent and convolutional neural networks and other deep learning architectures that have demonstrated reliable results to detect dental structures in preliminary tests.(22)

Radiographic Sample

Following protocol IRB approval (IRB # 18.1221), sixteen thousand (16,000) intraoral digital images tagged as right and left premolar and molar bitewings of patients attending the dental clinics at the University of Louisville School of Dentistry (ULSD) were retrieved from the image database (MiPACS Dental Enterprise Solution, Medicor Imaging, Charlotte, NC, USA) as anonymized, de-identified, uncompressed bit-mapped picture (BMP) images with no metadata attached. All images were acquired using a #2 size intraoral CMOS sensor (KODAK RVG 6100 System; Carestream KODAK Dental, Augusta, GA, USA).

Images were hand searched and the following exclusion criteria applied, eliminating 2,788 images:

1) Bitewing images depicting mixed or primary dentition
2) Non-bitewing images (e.g. periapical),
3) Non-dental images (e.g. photographic),
4) Images of inadequate diagnostic quality including;
   a) Over or underexposed images,
   b) Images demonstrating major positioning errors (e.g. cone cut), and
   c) Images demonstrating major geometric distortion errors (e.g. elongation and foreshortening).

The remaining 13,212 images were randomly assigned into four sets:

1) Training set - used to train the AI system on the identification and classification of dental caries (12,772 images);
2) Calibration set - used for training three experts and six evaluators with the use of the AI software interface (60 images);

3) Ground Truth set – presented to the experts and used to provide a consensus radiographic truth of the status of the proximal surface of the crowns of the teeth on the bitewing images (230 images), and;
4) Testing set - used to evaluate the performance of the system, and to compare it to the evaluators (150 images). The 'Testing set' of images were not seen by the system during the training phase.

The images were transferred to Denti.AI, Inc. via Amazon Web Services (AWS). Amazon Simple Storage Service (AWS s3) is a one of the many services offered by Amazon Web Services, Inc. which can be used for data storage, data analysis, data sharing and many other purposes. AWS services have multiple layers of operational and physical security to help ensure the integrity and safety of the data. The transfer of images through AWS is HIPPA compliant and the data is encrypted in transit and at rest.(26)

Machine Learning Software Interface

An online machine learning software interface, developed by Denti.AI, was used to visualize calibration, ground truth and testing image sets (Figure 1). For each digital bitewing image presented to the observer, between 5 to 15 proximal coronal surfaces were evaluated. Observers were asked to indicate the following:

Fig 1. Denti.AI Software Interface. Screenshot of Denti.AI interface shows annotation of the presence and location of proximal lesions (red rectangles) and tagging depth in right column (by experts only).

For each digital bitewing image presented to the observer, between 5 to 15 proximal coronal surfaces were evaluated. Observers were asked to indicate the following:

1) **Presence of Coronal Dental Caries.** All observers were asked to annotate the presence of proximal lesions by drawing a rectangular, bounding box covering the whole area of the dental carious lesion with margins not exceeding 2mm. Separate bounding boxes for each proximal location were drawn. When multiple lesions were located on the same tooth, and if the lesions were connected to each other, one bounding box including multiple locations was drawn. For proximal lesions affecting the surfaces of adjacent teeth, rectangles for each tooth were drawn with a possible intersection between the bounding boxes.

Observers were instructed to dismiss ambiguous radiolucent areas on proximal surfaces from assessment. This included teeth with failing restorations (voids, gaps, and other filling defects), surfaces where there was incomplete treatment or where restorations were missing, teeth demonstrating wear, tartar, and areas of cervical burnout at the cemento-enamel junction (CEJ).

2) **Location of Coronal Lesion.** Next, on teeth where lesions were detected and identified by a bounding box, observers were asked to indicate which surface was involved according to the following classes:
   a) Proximal surface – a lesion with immediate proximity to the contact area of an adjacent tooth surface.
   b) Non-proximal surface – any other non-proximal location, including occlusal, smooth, and root surface.
3) **Condition of Tooth Associated with Coronal Lesion.** Observers were then asked to indicate the condition of the tooth surface according to the following classes:
   a) Primary - a proximal lesion originating on a virgin surface, not associated with an existing restoration.
   b) Recurrent - a proximal lesion associated with an existing restoration. If the lesion is found around the margins of the restoration, it has to be tagged as "recurrent";
4) **Depth of Coronal Lesion**. Observers were then asked to indicate the depth of the proximal lesion according to the following:
   a) Incipient – enamel lesion less than halfway through the enamel.

b) Moderate – enamel lesion that penetrate at least halfway through enamel but that do not involve the dentino-enamel junction (DEJ).

c) Advanced – proximal lesion involving both the enamel and dentine definitely at or through the DEJ extending into the dentine less than halfway to the pulp cavity.

d) Severe – proximal lesion of enamel and dentine penetrating into the dentine more than halfway through the dentine towards, or including, the pulp cavity.

5) **Decision Confidence (Experts only).** In addition, the experts were asked to indicate their confidence in the presence of a proximal lesion using the following scale:

   a) C1 – Not Confident

   b) C2 – Slightly Confident

   c) C3 – Somewhat Confident

   d) C4 – Moderately Confident

   e) C5 – Very Confident

Viewing Conditions

The digital images in the Testing set and the Ground truth set were evaluated by the observers and experts respectively in a darkened room with no ambient lighting. The monitor used in this situation was a Dell Professional P2210H (Dell Inc., Round Rock, TX, USA) with 1920 x 1080 resolution. The monitor was calibrated using the TG10-QC calibration pattern to ensure the same image quality throughout.

Statistical Analysis

The testing data set of 150 images was used to evaluate the performance of the AI system and to compare it to the experts independently. All images were analyzed by both the AI system and the evaluators independently and annotations compared. When in disagreement, the ground truth annotations by experts were used as a reference to evaluate.

The sensitivity and specificity of each evaluator, for all evaluators and the Denti.AI software in the testing Data Set were calculated. For each image and each observer the following metrics are provided:

- True Positives - the number of teeth annotated both by the ground-truth experts and AI/specified observer(s);
- False Positives - the number of teeth annotated by the AI/observer(s) but not provided by the ground-truth expert(s);
- False Negatives - the number of teeth annotated by the ground-truth experts only;
- True Negatives - the number of teeth not annotated either by the ground-truth experts nor by the AI/observer(s).
- Sensitivity measures the proportion of actual positives that are correctly identified, which was measured by the formula:

$$\textit{Sensitivity} = \frac{\textit{number of true positives}}{\textit{number of true positives} + \textit{number of false negatives}}$$

- Specificity measures the proportion of actual negatives that are correctly identified, which was measure by the formula:

$$Specificity = \frac{number\ of\ true\ negatives}{number\ of\ true\ negatives + number\ of\ false\ positives}$$

The Area (Az) under the Receiver Operating Characteristic (ROC) curve was calculated using the Bootstrap method for both AI and all Observers at the significance of $p \leq 0.025$. Based on the bootstrap method, the observations of all the images from Testing set were collected and the observations were sampled randomly with replacements. Subsequently, the bootstrap version of the ROC AUC statistic was computed based on the initial sample size. The above mentioned two steps were repeated for a large number of times (1000 iterations were used as recommended in the literature).(27) Finally, the lower and upper bounds of the 95% Confidence Intervals (CI) were calculated based on the statistics collected for all the iterations.

CHAPTER III

RESULTS

Table 1 shows a comparison of various diagnostic performance measures including sensitivity, specificity and Az values for each observer individually and for all observers overall as compared to Denti.AI software for the detection of proximal lesions using a consensus Delphi derived truth. Observation of the true positive and false negative results for Observer 4 clearly indicate that this individual should be considered an outlier, poorly suited to the prescribed diagnostic task and, as such, were not subsequently included in the calculation of the overall performance measures.

Overall the Denti.AI software proximal lesion detection algorithm demonstrated greater sensitivity (0.624) than observers (0.530) however reduced specificity (0.715) than observers (0.884). Denti.AI software provided greater sensitivity for 4 of the 5 observers. There was no difference between Az for Denti.AI and observers. Examples of false positive and false negative detection errors for specific observers are illustrated for the Denti.AI algorithm in Figure 2 and Figure 3 respectively.

Table 1. Performance Measures Comparison. Comparison of various performance measures including sensitivity, specificity and Az values using the bootstrap method [97.5% confidence interval] for each observer individually and for all observers overall as compared to Denti.AI software for the detection of proximal lesions. ($p \leq 0.025$)

Performance Measure	AI	All Observers	Obs 1	Obs 2	Obs 3	Obs 4*	Obs 5	Obs 6
True Positive	171	114	32	14	21	8	25	22
False Positive	357	171	38	9	6	40	74	44
False Negative	103	101	11	29	22	35	18	21
True Negative	897	1,289	254	283	286	252	218	248
Sensitivity	**0.62**	**0.53**	0.74	0.33	0.49	0.19	0.58	0.51
Specificity	**0.72**	**0.88**	0.87	0.97	0.98	0.86	0.75	0.85
Az	0.70 (0.66-0.74)	0.71 (0.65-0.82)	0.82	0.65	0.74	0.53	0.66	0.69

Obs, Observer: Az, Area under the curve using receiver operating characteristic: AI, Denti.AI machine learning program: * Observer 4 removed from overall results: **Bold**, statistically significant differences detected

Table 2. Sensitivity for Various Proximal Lesion Depths. Comparison of sensitivity using bootstrap method for each Observer and all Observers as compared to AI for the detection of proximal lesions at various depths. (*p* ≤0.025)

Caries Depth	**AI**	**Observers combined**	**Obs 1**	**Obs 2**	**Obs 3**	**Obs 4***	**Obs 5**	**Obs 6**
Incipient	**0.51**	**0.27**	0.33	0.17	0.17	0	0.67	0
Moderate	**0.51**	**0.30**	0.50	0.13	0.38	0	0.38	0.13
Advanced	**0.40**	**0.46**	0.74	0.36	0.45	0.16	0.36	0.39
Severe	**0.58**	**0.75**	1.00	0.50	0.75	0.50	0.50	1.00

Obs, Observer: Az, Area under the curve using receiver operating characteristic: AI, Denti.AI machine learning program: * Observer 4 removed from overall results: **Bold**, statistically significant differences detected

Table 2 shows a comparison of sensitivity for each observer individually and for observers overall as compared to Denti.AI software for the detection of proximal lesions at various depths using a consensus Delphi derived truth. Compared to observers overall, the use of the Denti.AI algorithm provided significantly higher sensitivity for incipient (0.51) and moderately sized (0.51) proximal lesion detection but poorer sensitivity for advanced (0.4) and severe sized (0.58) lesions. Observers had a wide range of sensitivities for incipient (0.17 – 0.67) and moderate (0.13 – 0.50) sized lesions and were outperformed by the Denti.AI software algorithm for 4 of the 5 observers and all observers respectively.

Table 3 shows a comparison of sensitivity for each observer individually and for observers overall as compared to Denti.AI software for the detection of proximal lesions based on the type of lesions (primary vs. recurrent) using a consensus Delphi derived truth. For primary proximal lesions overall, the Denti.AI software caries detection algorithm demonstrated greater sensitivity (0.51) than observers (0.43), providing greater sensitivity for 4 of the 5 observers. However, while the specificity for Denti.AI software specificity was significantly lower for secondary, recurrent proximal lesions (0.39) than observers overall (0.45), it outperformed 2 of the 5 observers.

Table 3. Sensitivity based on type of lesion. Comparison of sensitivity using bootstrap method for each Observer and all Observers as compared to AI for the detection of primary and recurrent proximal lesions. (*p* ≤0.025)

Type	**AI**	**All Observers**	**Obs 1**	**Obs 2**	**Obs 3**	**Obs 4***	**Obs 5**	**Obs 6**
Primary	**0.51**	**0.43**	0.63	0.25	0.50	0.16	0.41	0.34
Recurrent	**0.39**	**0.45**	0.77	0.41	0.29	0.12	0.41	0.35

Obs, Observer: Az, Area under the curve using receiver operating characteristic: AI, Denti.AI machine learning program: * Observer 4 removed from overall results: **Bold**, statistically significant differences detected

Fig 2. Proximal lesion detection errors produced by the system (AI). For each case, the left image shows the boxes annotated by the experts – ground truth, the right image shows the boxes detected by the system. False positives: 2a., 2b.

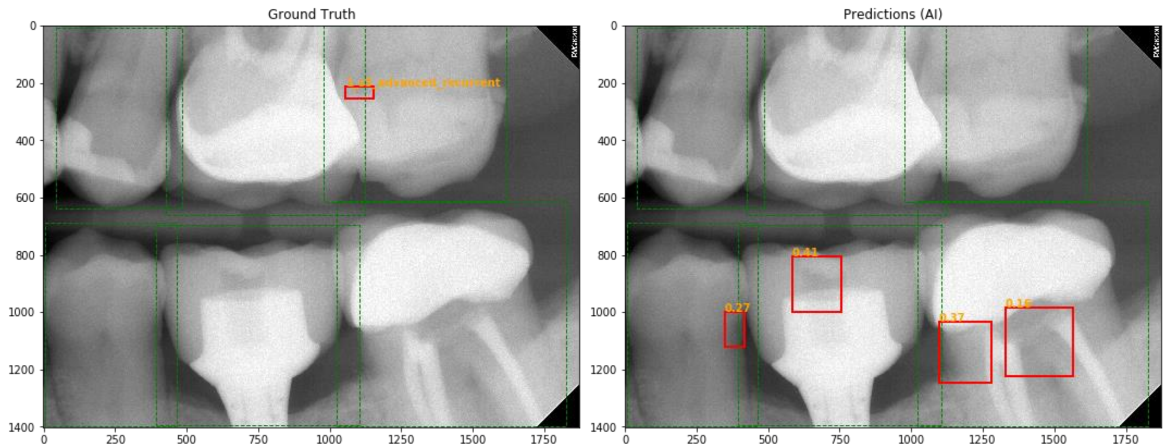

Figure 2a – Example 1 of a False Positive

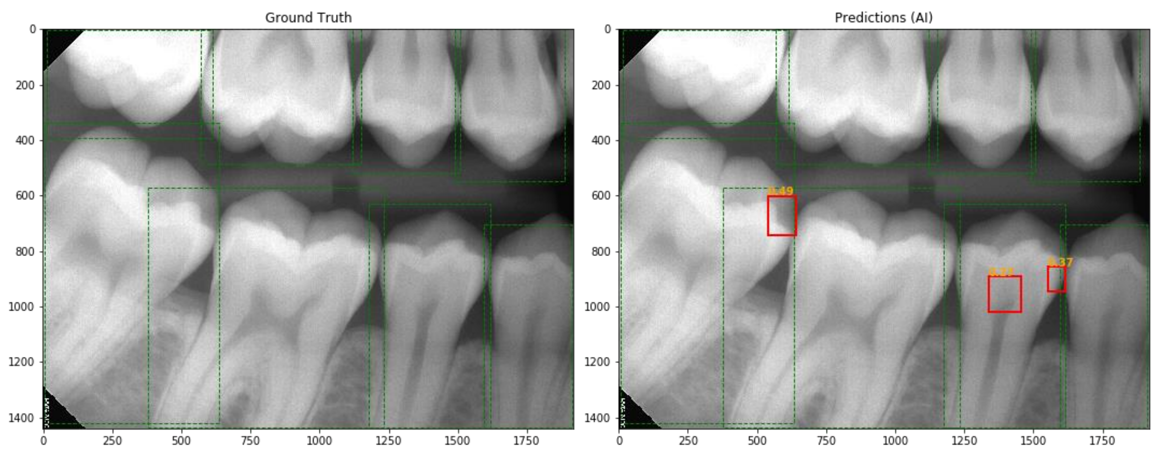

Figure 2b – Example 2 of a False Positive

Fig 2. Proximal lesion detection errors produced by the system (AI). For each case, the left image shows the boxes annotated by the experts – ground truth, the right image shows the boxes detected by the system. False negatives: 2c., 2d.

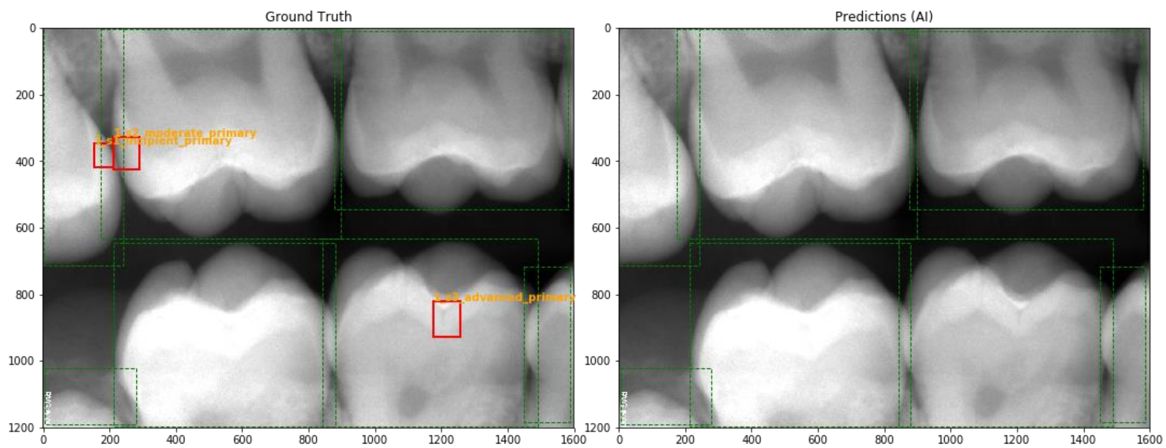

Figure 2c – Example 1 of a False Negative

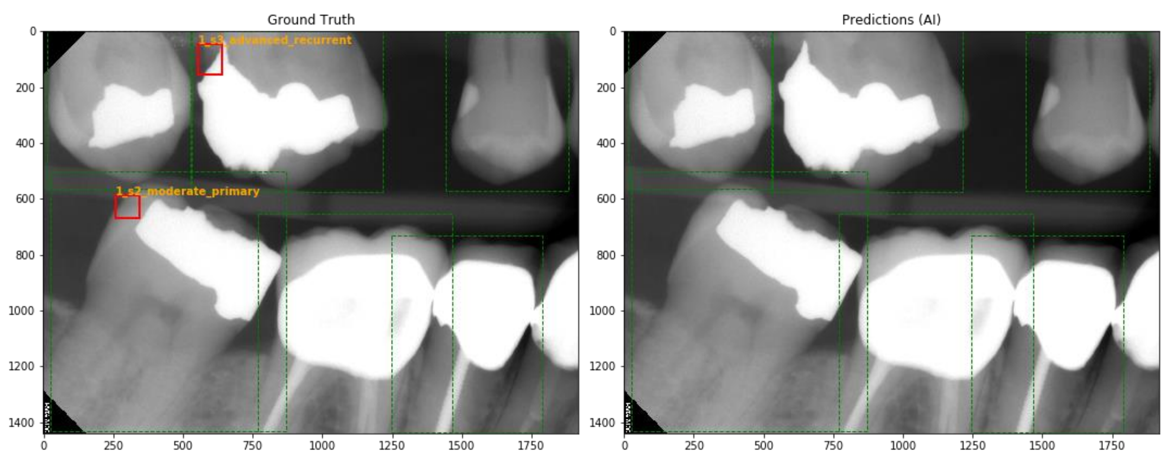

Figure 2d – Example 2 of a False Negative

Fig 3. Proximal lesion detection errors produced by a representative observer. For each case, the left image shows the boxes annotated by the experts – ground truth, the right image shows the boxes detected by the observer(s). False positives: 3a., 3b.

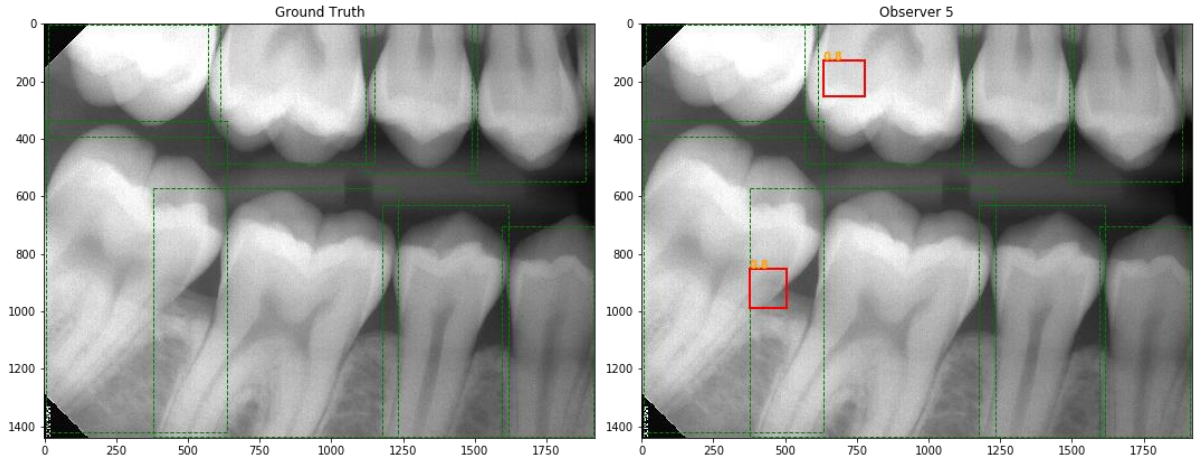

Figure 3a – Example 1 of a False Positive for Observer 5

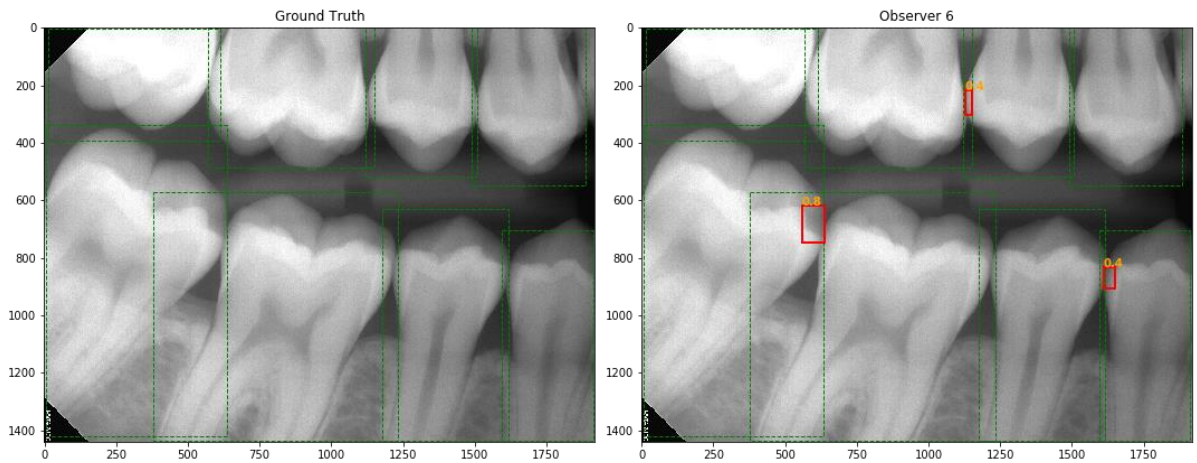

Figure 3b – Example 1 of a False Positive for Observer 6

Fig 3. Proximal lesion detection errors produced by a representative observer. For each case, the left image shows the boxes annotated by the experts – ground truth, the right image shows the boxes detected by the observer(s). False negatives: 3c., 3d.

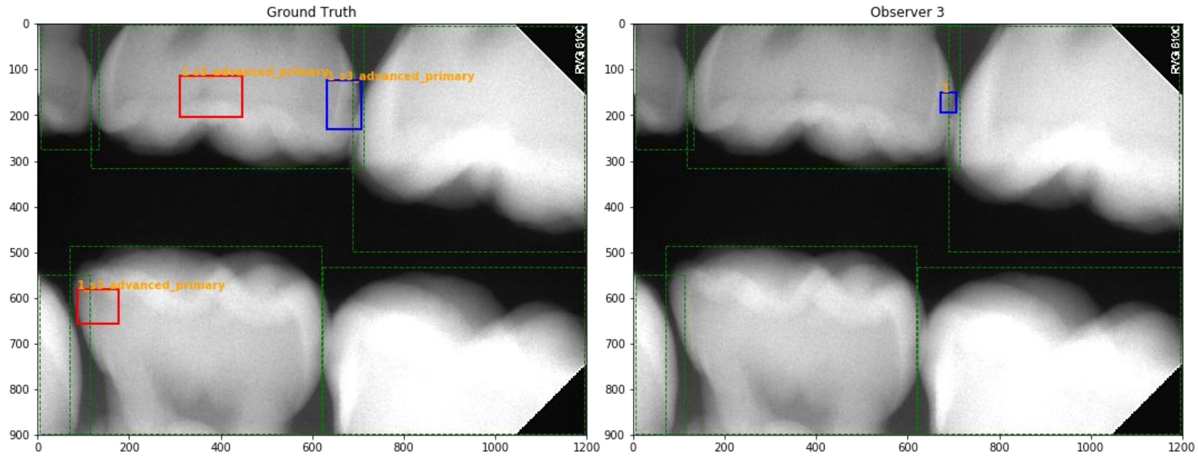

Figure 3c – Example 1 of a False Negative for Observer 3

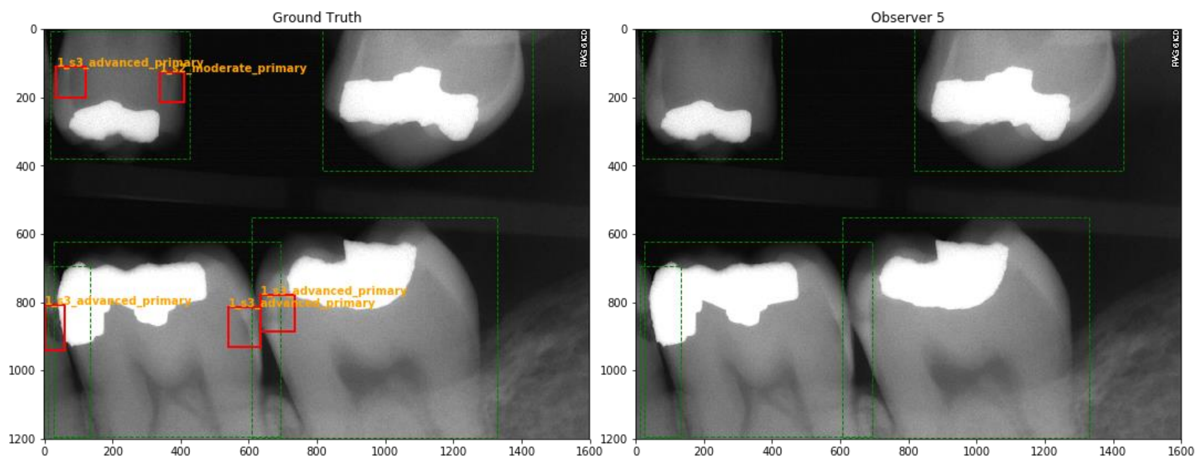

Figure 3d – Example 2 of a False Negative for Observer 5

CHAPTER IV

DISCUSSION

Over the last decade, artificial intelligence learning systems have become increasingly popular, demonstrating promising results when rendering image-related decisions in medicine. Their application in healthcare could allow more comprehensive, reliable, and precise image assessment and diagnostics, facilitating better patient care. In the present study, the potential of AI is applied to Dentistry for an automated detection of proximal dental caries detection on digital bitewing images in vivo. The system was applied to both high-quality images with normal teeth arrangement and more challenging cases such as overlapped or impacted teeth, images of poor quality with blurred contours of teeth, teeth with large restorations, crowns and bridges and restored implants.

Overall the AI system achieved similar accuracy for proximal dental caries detection compared to observers, increasing sensitivity but providing reduced specificity. The accuracy of the AI system performed better for three of the 5 observers. However, observers' performance on correctly detecting when the tooth is sound and no carious lesion is present (i.e. specificity), was markedly greater than the AI system. The sensitivity and specificity of digital intraoral radiography compared to a gold standard for the detection of interproximal caries ranges on the depth of the lesion and imaging modality. While sensitivity for observers (0.53) and the AI system (0.62) in the present study are comparable to published values (0.45 – 0.55)(28) , the specificity values for both observers

(0.88) and the AI system (0.72) are reduced compared to those reported in the literature (> 0.9).(29, 30) Therefore, application of the system into the digital workflow in clinical practice should be considered with caution with higher accuracy for most observers achieved at the expense of over diagnosis.

There were certain limitations in the current study that should be considered before applying these results to clinical practice. The first was that the current study involved a comparison of the AI system's diagnostic performance trained using a Delphi consensus of truth of three oral and maxillofacial radiologists vs. human observers on images. The true condition of each proximal surface of the teeth was not verified using clinical examination. Secondly it is unknown whether the proximal lesion was demineralization based on microbial activity (dental caries) or erosion based on the localized presence of acids from ingestion or regurgitation. Thirdly, the currently accepted method of establishing a golden standard of carious status is by histological assessment in addition to clinical and radiological evaluations. Since the study was performed using images obtained retrospectively, a histological assessment was not feasible. As this is a proof-of-concept study, the comparison was made between application of the AI system and human observers' diagnostic performance independently. A further study would be advisable using two groups of observers; one group without access to the results of the AI system and a second group who have access to the results of the AI system. In this design, the effect of an AI system to supplement radiologic detection observation could be investigated. In addition, our study did not measure or control for the amount of time spent by each observer in the process of interpretation; further studies of human observer performance in this task where observers have access to the results of the AI system prior to interpretation should include considerations of work efficiency.

Furthermore, a Kappa (κ) statistical analysis is usually performed as a measure of an agreement to determine the inter- and intraexaminer reliability among the involved observers. However, in the current study, the reliability was not measured since AI was one of the observers along with other human observers and since it learns to detect proximal lesions based on expert human observer inputs. κ-values are categorized as low ($\leq$0.40), moderate (0.41 to 0.60), good (0.61 to 0.80) and excellent agreement (0.81 to 1.00).(31) Litzenburger et al. (2018) report κ-values for digital bitewing radiography for proximal caries detection are good; Inter: κ = 0.63 (0.60-0.67) and Intra κ = 0.64 (0.61-0.67).(32) Finally, the dataset used in the current study included permanent teeth only; it did not include images with deciduous teeth or images demonstrating individuals in the mixed dentition phase. Images with deciduous teeth were specifically excluded considering the different morphology of the crowns of these teeth. The AI system will therefore require additional training to detect and identify the primary dentition accurately. Hence, a further study is necessary by training the system with a much larger dataset since the higher the number of subjects used to train the neural network, the higher the accuracy it will have for testing unknown objects.

Deep learning techniques can be applied to numerous other tasks than carious detection. Several exciting prospects are currently being studied, for example, using machine learning technologies to detect pathologies, such as periodontitis and periapical cysts. Admittedly, to achieve expert-level results for such a task, these new systems would require larger datasets for training than used in this project.

CHAPTER V

CONCLUSION

The higher sensitivity of AI for detecting proximal lesions compared to observers, particularly for smaller lesions, suggests that the AI system is valuable for detecting density variations on the proximal surfaces of bitewing images. However, low specificity values imply that further training with a more extensive data set is needed to improve and make the system more robust to differentiate proximal lesions from "look-alike" entities such as cervical burnout and artifacts.

AI deep learning algorithms have a potential for further investigation of their applications and implementation in a clinical dental setting. While it is being trained based on the input from oral radiology experts around the world, it is not prone to human factors such as eye fatigue, gray-scale smoothening, and conformational bias. Finally, it is of our opinion that the purpose of AI is not to exclude the input of the clinician from the process of radiographic dental caries diagnosis but to highlight suspicious areas, increasing clinical efficiency by focusing human effort towards specific sites that need further evaluation.

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