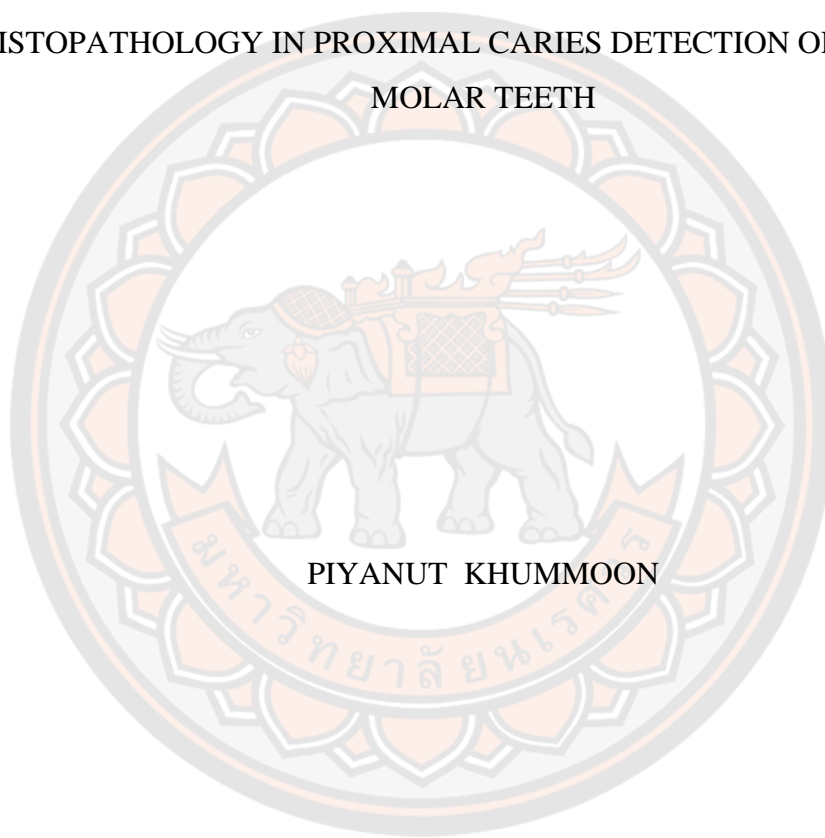




ACCURACY OF EXTRAORAL BITEWING COMPARED WITH
HISTOPATHOLOGY IN PROXIMAL CARIES DETECTION OF PRIMARY
MOLAR TEETH



PIYANUT KHUMMOON

A Thesis Submitted to the Graduate School of Naresuan University
in Partial Fulfillment of the Requirements
for the Master of Science in Master of Sciences in Dentistry (Pediatric Dentistry) -

Type A 2

2023

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Thesis entitled "Accuracy of extraoral bitewing compared with histopathology in proximal caries detection of primary molar teeth"

By Piyanut Khummoon

has been approved by the Graduate School as partial fulfillment of the requirements for the Master of Science in Master of Sciences in Dentistry (Pediatric Dentistry) - Type A 2 of Naresuan University

Oral Defense Committee

..... Chair
(Assistant Professor Paiboon Jitprasertwong, Ph.D.)

..... Advisor
(Assistant Professor Sirilawan Tohnak, Ph.D.)

..... Co Advisor
(Assistant Professor Chutamas Deepho, Ph.D.)

..... Internal Examiner
(Assistant Professor Ruedee Sakulratchata, Ph.D.)

Approved

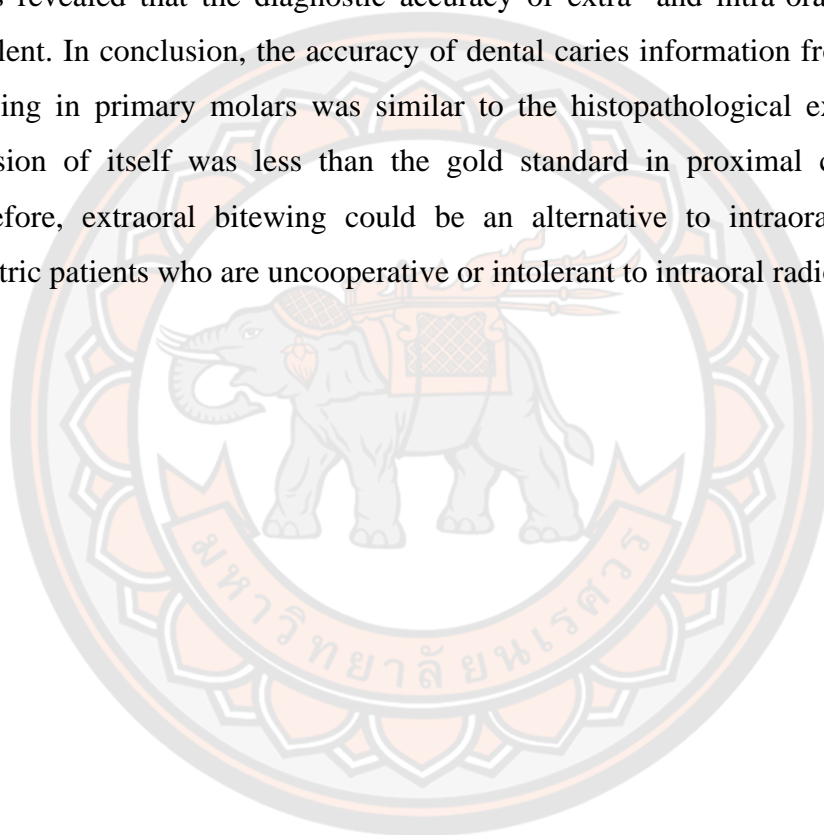
.....
(Associate Professor Krongkarn Chootip, Ph.D.)
Dean of the Graduate School

Title	ACCURACY OF EXTRAORAL BITEWING COMPARED WITH HISTOPATHOLOGY IN PROXIMAL CARIES DETECTION OF PRIMARY MOLAR TEETH
Author	Piyanut Khummoon
Advisor	Assistant Professor Sirilawan Tohnak, Ph.D.
Co-Advisor	Assistant Professor Chutamas Deepho, Ph.D.
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ABSTRACT

Proximal caries detection in pediatric patients is critical for a suitable treatment plan and prevents premature loss of deciduous teeth. Using direct visual examination alone may not be able to yield an accurate diagnosis for proximal caries. Intraoral bitewing radiography is an additional method that helps determine proximal caries. However, some limitations of the intraoral radiograph technique cannot be compatible with some patients and might lead them to become uncooperative. Extraoral bitewing radiography overcomes the issue of patients who refused to undergo intraoral radiographs. Our research study aimed to compare the accuracy of extraoral bitewing radiography and histopathological examination for proximal caries detection in the primary molars. Fifty-six extracted primary molars with and without proximal caries were divided into seven groups. Each group was arranged in the mimetic alveolar sockets of a 3D-printed skull and mandible. Intraoral bitewing was taken with photostimulable phosphor (PSP) plates size 0 using the paralleling technique. Extraoral bitewing was obtained using a digital panoramic X-ray unit. Two observers were evaluated extraoral bitewing radiographs separately, twice at one-week intervals, to minimize the possibility of recalling their previous assessments. The weighted kappa coefficients showed excellent intra- and inter-observer

agreements between each observer. The Mann-Whitney U test showed no difference between the radiographic grading scores and the gold standard histological examination. The Wilcoxon signed-rank test showed the differences between intra- and extra-oral radiographic modalities were insignificant. The sensitivity, positive predictive value (PPV), negative predictive value (NPV), and the area under the receiver operating characteristic (ROC) curve of both observers for cavitated carious lesions were higher than non-cavitated carious lesions. The Az value for cavitated caries revealed that the diagnostic accuracy of extra- and intra-oral bitewings was excellent. In conclusion, the accuracy of dental caries information from the extraoral bitewing in primary molars was similar to the histopathological examination. The precision of itself was less than the gold standard in proximal caries detection. Therefore, extraoral bitewing could be an alternative to intraoral technique for pediatric patients who are uncooperative or intolerant to intraoral radiography.



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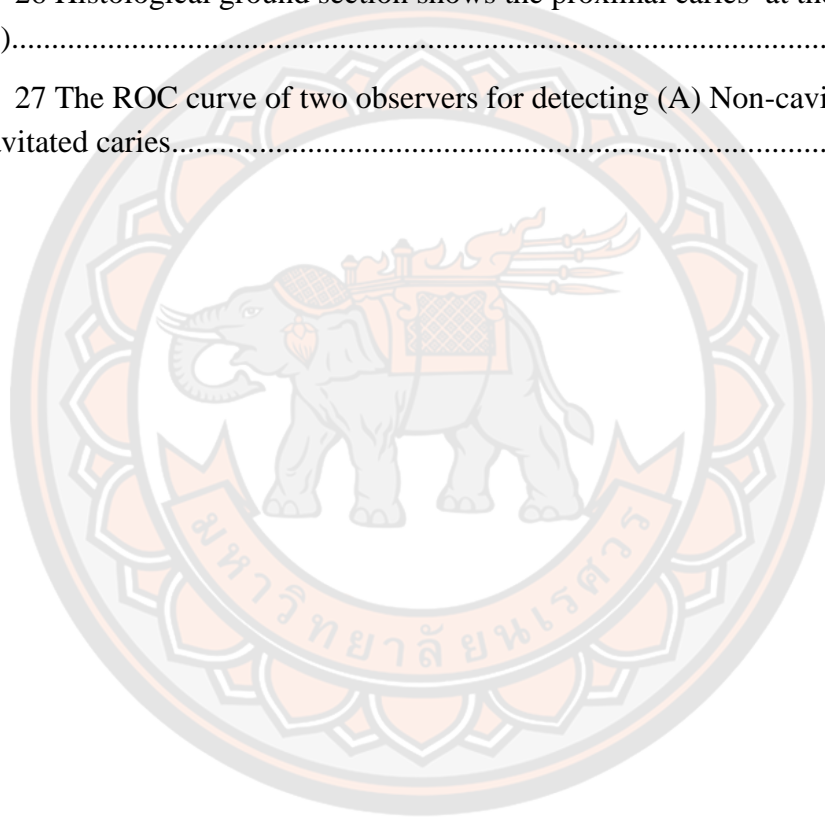
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Thesis proposal

Title Accuracy of extraoral bitewing compared with histopathology in proximal caries detection of primary molar teeth

1. Background and Significance of the Study

Dental caries is a multifactorial disease caused by the imbalance of the demineralization and remineralization process. It is referred to as a pandemic disease because it affects a large number of people. Untreated dental caries from both deciduous and permanent teeth can cause infection, oral pain, more complex and costly treatments, especially early tooth loss in children. (1, 2) The most effective method for preventing the progression of the carious lesion is early detection. Only clinical examination is insufficient for proximal caries detection and results in a misdiagnosis.

The radiographic examination can be performed either intraorally or extraorally. (3) Intraoral bitewing radiographs are often utilized worldwide to identify proximal caries. On the other hand, intraoral bitewing leads to patient discomfort and requires various skill levels of the assistants. The overlapping appearance of the interproximal surface also complicates the diagnosis of proximal caries. (4, 5, 6) Intraoral bitewings can transmit respiratory diseases such the Coronavirus disease (COVID-19) by evaporating saliva and respiratory secretions or droplets while the child speaks, coughs, sneezes, or sobs. (7, 8) Regarding the pandemic of COVID-19 recently, extraoral bitewing radiography has prominently increased as a means of overcoming respiratory diseases transmission during intraoral bitewing radiographs taken.

Extraoral bitewing radiographs reveal the entire crown and root structures of the maxilla and mandible. (5, 6, 9, 10, 11) There are advantages in providing a complete image of both left and right posterior teeth with single radiation exposure. (12) Several *in vivo* and *in vitro* studies, comparing extraoral bitewing radiographs to other modalities such as intraoral bitewing radiography, panoramic radiography, and CBCT, determined the diagnostic accuracy of proximal caries detection in permanent teeth. The results indicated no differences in diagnostic accuracy among these modalities. (5, 6, 11) Additionally, the extraoral bitewing technique potentially revealed initial proximal caries similar to the intraoral bitewing technique (13) and detected more carious lesions and bone loss findings than intraoral bitewing radiographs. (10) An application of the extraoral bitewing to identify dental caries in different tooth morphology, especially in primary dentition, is a great challenge. Currently, the accuracy of extraoral bitewing radiography in detecting proximal caries of primary teeth is ongoing. Therefore, we intend to investigate the accuracy of the extraoral bitewing in dental caries detection in primary molar and compare it with histopathological examination utilizing the gold standard.

2. Research Aim

To compare the accuracy of the extraoral bitewing radiography with histopathological examination for proximal caries detection in the primary molar.

3. Research Significance

3.1 This study is pioneer research to test the accuracy of extraoral bitewing in primary molars embedded in 3D printing jaws. A comparison of the accuracy of extraoral bitewing with intraoral bitewing may be applied in clinical practice.

3.2 The accuracy of extraoral bitewing radiographs can be helpful for dental practitioners to decide on a pediatric dental treatment plan.

4. Scope of the Research

This ex-vivo study will be performed on the human primary molar, gathered from the pediatric dental clinic, faculty of dentistry, Naresuan University, and several private dental clinics, in Phitsanulok, Thailand. The samples will be set up in the 3D jaw model. The extraoral bitewing radiographs will be taken prior to the histopathological examination.

5. Keyword

Extraoral bitewing radiographs, bitewing radiographs, proximal caries, proximal caries detection, pediatric radiographs

6. Research hypothesis

H0: Accuracy of the extraoral bitewing in dental caries detection in primary molar is similar to histopathological examination

H1: Accuracy of the extraoral bitewing in dental caries detection in primary molar is different from histopathological examination

7. Literature Review

Dental caries and etiology of caries

Dental caries is the consequence of the disease and affects both children and adults. It is also the main cause of oral pain and early tooth loss in childhood. Dental caries is a multifactorial disease that is preventable. The disease development process is basically caused by an imbalance between pathological and protective factors. The factors contributing to the development of dental caries are illustrated in Figure 1 (1, 2, 14, 15).

Dental caries procession is influenced by a variety of risk and preventive factors. Reduced salivary function, such as buffer capacity and pH, results in demineralization underneath the tooth structure. Furthermore, oral hygiene, heredity, tooth anatomy, dentin and enamel composition, fluoride prescription, chemotherapeutics agents, and socioeconomic status are all considering factors (1, 2, 14, 15, 16).

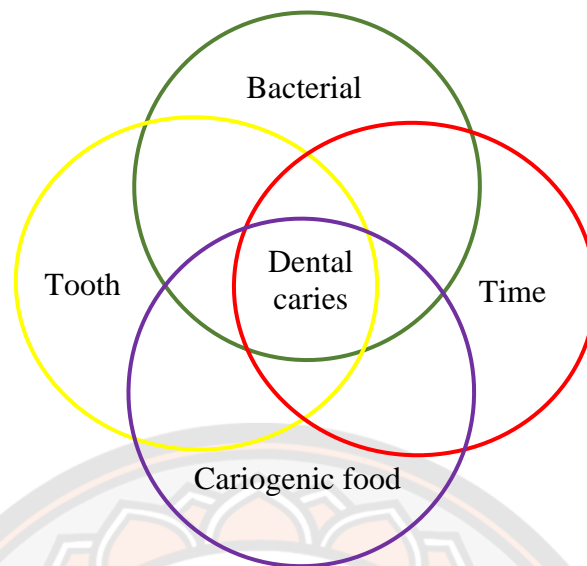


Figure 1 The factors that contribute to the development of dental caries, as modified by Selwitz Robert H, et al. 2007 (2)

An imbalanced diet, for example low fruit and vegetable intake and high cariogenic food intake, speedily leads to the tooth demineralization process. The acid formation, a result of carbohydrate fermentation of microorganisms to cariogenic food, causes oral pH reduction impacting both the biofilm composition and the mineral loss of the tooth surface. A prolonged low pH period increases microbial population toward acidogenic and acidophilic bacteria in the biofilm. This, in turn, will contribute to increased acidification and demineralization of the environment. For the tooth structure, low pH periods gradually cause mineral loss from the enamel and dentin structure. When the pH of the biofilm returns to neutral, and the concentration of soluble calcium and phosphate is saturated, minerals are reintroduced into decalcified enamel. This is referred to as remineralization. The dental caries procedure at the tooth surface and subsurface level is a dynamic process between demineralization and remineralization, moderated by risk factors and preventive factors. Recognizing the equilibrium between demineralization and remineralization and risk factors is an important issue for caries management (Figure 2) (1, 15, 17).

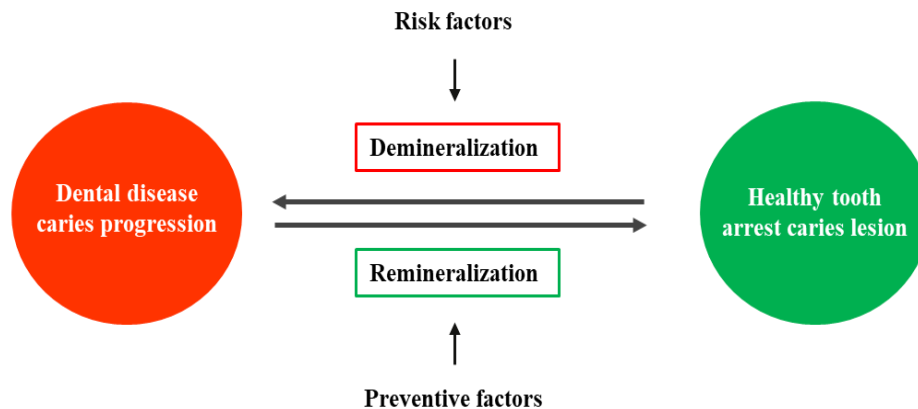


Figure 2 A dynamic process of demineralization and remineralization in the tooth of dental caries lesions, as modified by Pitts, Nigel B., et al. 2017 (17)

Early childhood caries is defined as dental caries occurring before the child reaches the age of 71 months. The carious lesion can develop on the smooth, occlusal, or proximal surfaces of a child's first teeth. It affects the enamel, dentin, and cementum. Dental caries starts with dental plaque covering the demineralized tooth surface that is either undetectable during clinical examinations and radiographic examinations or observable as a white spot lesion after plaque removal (Figure 3). The initial stage of the disease can be reversed by increasing remineralization through fluoride toothpaste brushing and topical fluoride application. Dental caries can be prevented, arrested, and restored with adequate control or monitoring of risk factors. However, if the demineralization persists, the surfaces of the white spot progress to a cavitated lesion. If left unattended, it will cause severe damage to the tooth structure and possibly early tooth loss (2, 14, 15) (Figure 4).



Figure 3 The initial stage of dental caries (By the author)



Figure 4 The severe stage of dental caries (By the author)

Pathology of dental caries

Dental caries is a disturbance of the physiological balance between the demineralization and remineralization process. Oral microorganisms have been considered as the major virulence of caries-producing organisms. The main cause of dental caries is *Streptococcus mutans*, which is an acidogenic bacterial species. They initially attach to the acquired pellicle, a film of proteins and glycoproteins on the tooth surface, forming dental plaque known as a biofilm (2, 14). Additional microbial species accumulations, such as *Streptococcus sobrinus*, lactobacilli, and bifidobacteria, have been associated with the later stage of dental caries development. Secondary colonizing species adhere to the initial colonizers, generating ambiguity in the biofilm. Oral biofilms contain approximately 700 different species of bacteria, and their diversity exceeds that of carious teeth (16, 18). Tooth cleansing is necessary to control biofilm and prevents dental caries. After the biofilm removal from the tooth surface, a new layer of biofilm is assembled within two hours (15, 17). Biofilm produces weak acids as a result of the metabolism of fermentable carbohydrates. This acid tends to lower the pH level below a critical level, which results in demineralization and cavitation of tooth structures. Increasing carbohydrate or sugar consumption develops dental caries rapidly. Dental caries is a dynamic process, involving both demineralization and remineralization (2, 16). Saliva has a buffering capacity, which enables it to promote acid neutralization, provides additional calcium and phosphate to the tooth subsurface, and reduces the dental plaque's cariogenic activity (1, 16, 17). The dentists need to critically understand the pathogenesis of dental caries in order to provide an individual prevention and treatment plan.

Dental caries in primary teeth

The characteristics of dental caries in primary teeth are distinctive from those in permanent teeth. Primary teeth start to erupt at 6-months and completely erupt at the age of 2 to 3 years, so dental caries can occur as soon as teeth erupt. Carious lesions in children are commonly found in the maxillary anterior teeth, the occlusal surface, and the smooth surface, especially the proximal surface, of posterior teeth (15, 19).

The etiology of dental caries in the maxillary anterior teeth varies by country. In developed countries, etiology is associated with improper use of the feeding bottle

and sleeping with the bottle or nipple in their mouth. However, it is associated with malnutrition, inaccessibility to dental services, and neglect of children's oral health in developing countries (19, 20).

Occlusal caries is the most common type of caries found in the oral cavity and are present on the occlusal surface, which allows microorganisms to settle. However, it is easily detected, cleaned, and protected by sealant on this surface after tooth eruption (15).

Proximal caries, which occur at the contact surface of two adjacent teeth, are the second most commonly diagnosed type of caries. The proximal areas are in close contact making them difficult to clean. This contributes to the formation of caries in this area. Proximal caries lesion starts from enamel at proximal contact parallel to the dentin-enamel junction and progresses into the pulp chamber (15). Early detection of dental caries is important for early recognition and intervention, as well as for providing an appreciated treatment plan.

The prevalence of dental caries in primary teeth was 46.2% worldwide, varying considerably across continents. The Asian continent has the second-highest prevalence of dental caries in primary teeth (52.6%), after the African continent (53.1%) (21). Although occlusal caries is the highest prevalence among other types of primary tooth decay (82%), it can be easily detected by parents and dentists. Proximal caries is the second most common type of primary tooth decay (71.2%). The mesial surface of the primary second molar (35.5%) and the distal surface of the primary first molar (33.3%) were the most impacted surfaces. Proximal carious lesions in posterior teeth are invisible and inaccessible in pediatric patients due to the small size of the oral cavity. As a result, it becomes increasingly prevalent as one age (20, 22).

Characteristics of primary teeth

The complete deciduous dentition consists of twenty teeth divided into five groups. Each jaw quadrant includes two incisors, one canine and two molars. The primary molar, especially the second primary molar, is similar to the first permanent molar. In clinical characteristics, primary molars are more prominent and whiter than permanent molars. The enamel and dentin of the primary molars are approximately half the thickness of those of the permanent teeth, while the pulp to crown ratio of primary teeth is larger than that of the permanent teeth (Figure 5). Additionally, the contact surfaces of primary molars are flat and very broad buccolingually as a contact area, whereas permanent teeth contact areas have the characteristics of the permanent teeth as a contact point and the primary teeth consist of lower mineral content than permanent teeth. As a result, the occurrence of dental caries in primary teeth is more rapidly progressive than it does in permanent teeth (23, 24, 25).

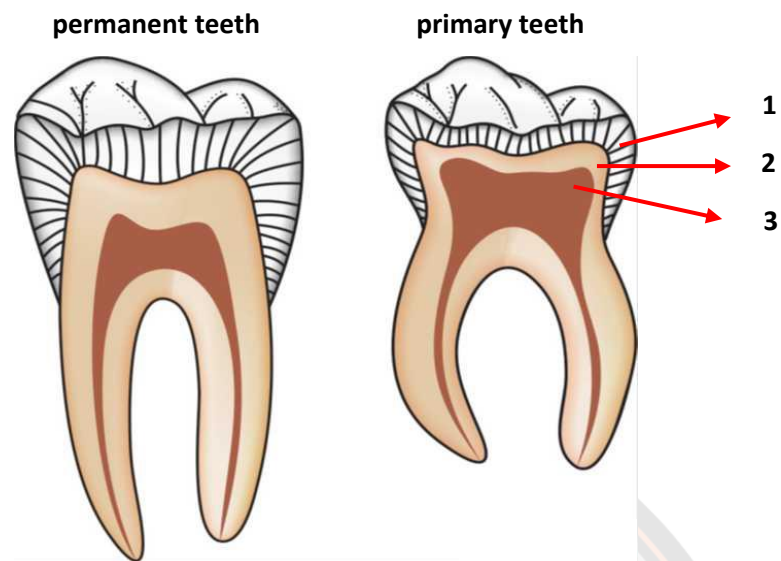


Figure 5 Characteristics of teeth in the primary teeth

- 1: The enamel of primary teeth is thinner than permanent teeth
- 2: The dentin of primary teeth is thinner than permanent teeth
- 3: The pulp to crown ratio of primary teeth is larger than that of the permanent teeth as modified by Turner Erwin G, Dean Jeffrey A, 2015 (25)

Enamel caries lesion on approximal surface

The proximal surfaces are prone to dental caries formation due to the higher accommodation available to cariogenic biofilm. The initial lesions develop beneath the contact surface and then become chalky white and opaque in areas determined by the shape of the gingival margin. The development of non-cavitated enamel caries lesions, also called white spot lesions, is the first clinical sign of demineralization (Figure 3). Histopathological sections illustrate an opaque wedge-shaped defect that starts at the enamel surface and extends toward the dentino-enamel junction (DEJ). The metabolic activity of bacteria within the lesion rapidly increases the dentin demineralization when the enamel cavitation occurs after DEJ demineralization (Figure 6-7) (15, 26, 27).



Figure 6 A white spot lesion appears as an opaque wedge-shaped defect. (27)

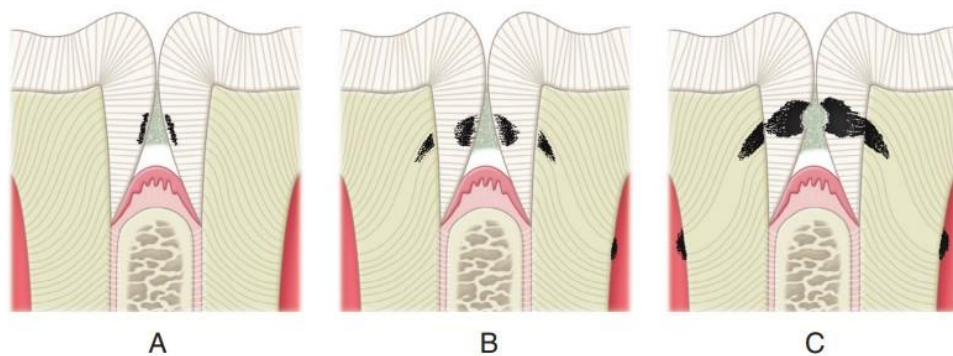


Figure 7 The initiation and progression of caries on interproximal surfaces.
 A: The lesions develop right below the contact surface and become chalky white and opaque, also called white spot lesions.
 B: The lesions progress toward the DEJ and are initially visible radiographically.
 C: The cavitated lesion can result in rapid demineralization of dentin. (15)

Dentin caries lesion on approximal surface

A carious lesion in dentin is more invasive than enamel because of low mineral content and the dentinal tubule structure. Carious lesions progress along the DEJ toward the pulp. Tubular sclerosis, also called the translucent zone, is the first sign of the pulp's defense reaction and can be found even before bacterial invasion into the dentin. The dentinal tubule deposits minerals which are visible under light microscopy. The superficial layer of the dentin is filled with bacteria and contamination. This zone is referred to histologically as the zone of necrosis and contamination, which clinically appears as soft dentin. Between the zone of bacterial contamination and the translucent zone is a zone of demineralization caused by bacteria's acid products and manifests clinically as a yellow-brownish discoloration of

the dentin. It is clinically presented as leathery dentin. In advance of caries lesion, the pulpal reaction develops as a protective mechanism by forming the tertiary dentin along the pulp wall (Figure 8-9) (15, 26).

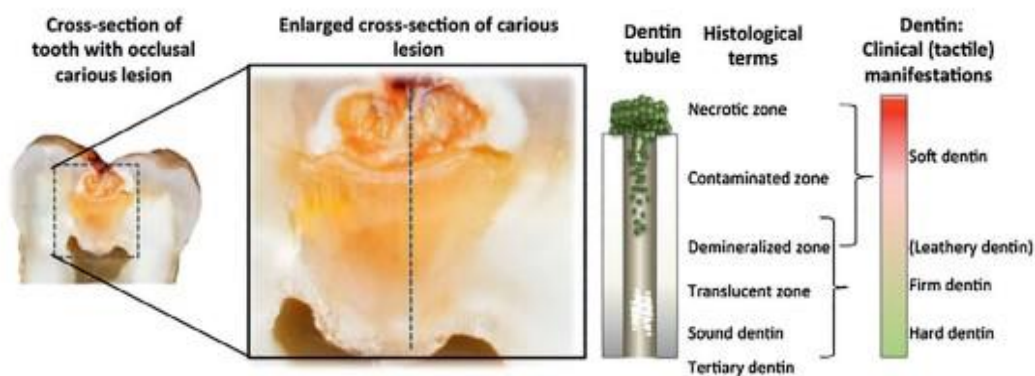


Figure 8 The histologic and clinical manifestations of dentin caries in different zones of dentin. (15)

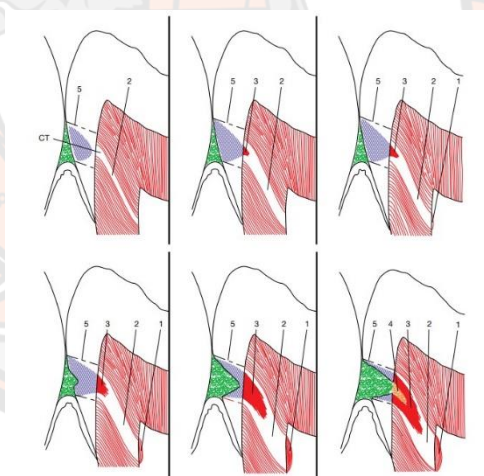


Figure 9 Schema of dental caries progression from enamel to dentin layer. (26)

Dental caries detection and assessment

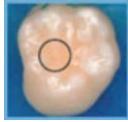

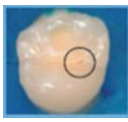
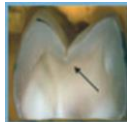



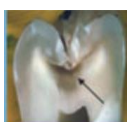

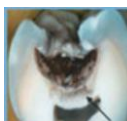
Dental caries detection is typically determined visual-tactile with a ball-ended probe. This method has many advantages, including the absence of additional tools, greater convenience, and patient acceptance. However, some studies indicated that the visual-tactile method was 42% sensitive for occlusal caries and 12–50% sensitive for proximal caries lesions (28).

Following that, visual detection criteria are developed for clinical use to describe stages of the caries process. The International Caries Detection and Assessment System (ICDAS) is one of the criteria providing clinical considerations

for dental caries management. Various ICDAS scores depend on the level of clinical appearance. There are 7 codes ranging from 0 to 6 (28, 29).

The ICDAS is a histologic-based methodology for detecting coronal caries. ICDAS scores of 3 or 4 indicate that demineralization has reached the middle 1/3 (approximately 67%) of the dentin, while the ICDAS score at 5 and 6 indicates the histological demineralization at the inner third or close to the pulp, approximately 84% of the dentin. Thus, there is a significant relationship between ICDAS scores and histology for both primary and permanent teeth, as shown in Table 1 (28, 30, 31, 32).

Table 1 ICDAS codes classifying caries progression based on histological evidence of lesion. (30, 31, 32)

ICDAS Score	Histology	Description
0 		No sign of demineralization
1 		Enamel demineralization limited to the 1/2 outer of the enamel
2 		Demineralization involving between 1/2 inner of the enamel and the 1/3 outer of dentine
3,4 		Demineralization involving the 1/3 middle of dentine
5,6 		Demineralization involving the 1/3 inner of the dentine

The American Dental Association Caries Classification System (ADA CCS)

The American Dental Association (ADA) established the ADA Caries Classification System (CCS) in 2015 for clinical use. The ADA CCS provides simple criteria to assess risk and to make decisions about effective therapeutic interventions for carious lesion management. An important issue of the ADA CCS is the capacity to classify a caries lesion in terms of the possibility of infected dentin. This probability benefits a caries management system that takes treatment into account. The clinical examination on occlusal and smooth tooth surfaces enables the clinician to assess the lesion directly visually and tactilely on a cleaned and dried tooth with appropriate light. For the proximal surface, visual and tactile methods can be possible with full visualization. Radiographic examination is a requirement when limited direct access occurs due to close contact between teeth. To improve overall patient health via improved oral health, the ADA CCS simplified the process of evaluating the effectiveness of caries control approaches in clinical practice. The characteristics of both clinical appearances with ICDAS codes combined with radiographic appearances correctly determine the progression of the carious lesion (28, 33) (Table 2).

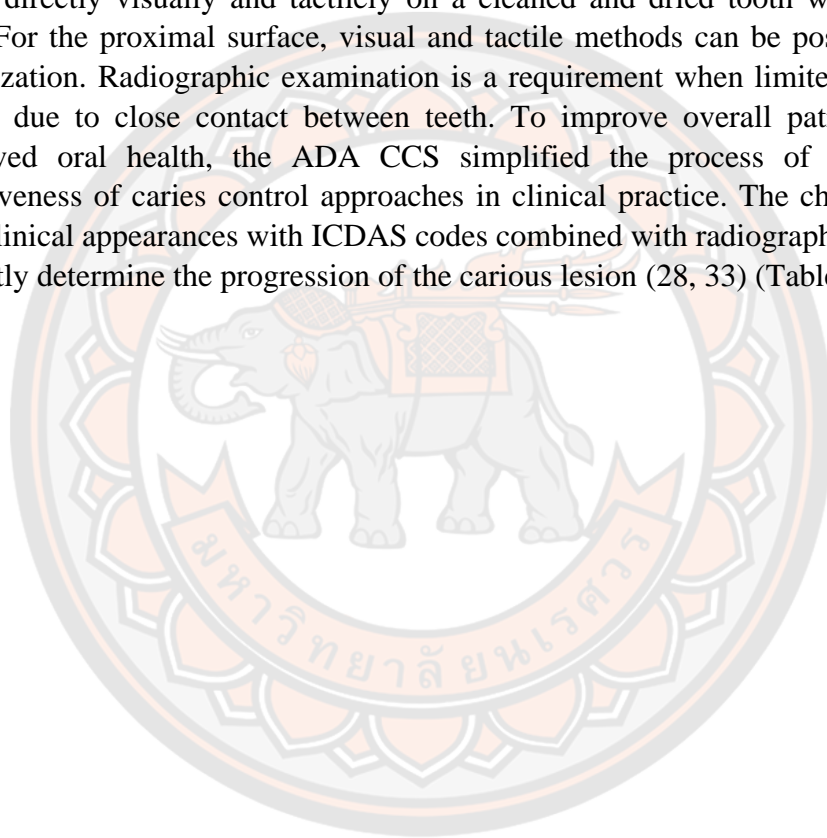

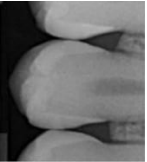
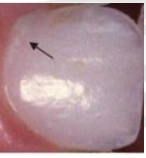
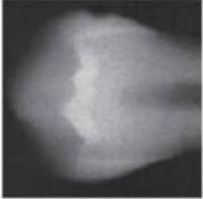
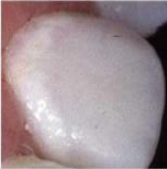
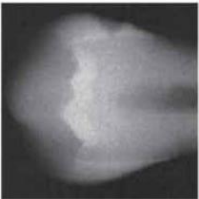


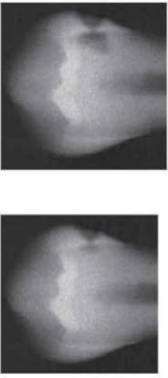

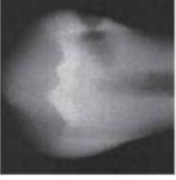

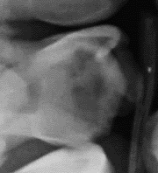


Table 2 The definition of ICDAS codes with clinical and radiographic appearances, as modified by ADA CCS 2015 (29, 33)

ICDAS Code	Description	Clinical appearances	Radiographic appearances
0 Sound tooth	No clinical change in tooth surface after prolonged air drying for 5 seconds.		
1 First visible change in enamel	Detecting only after prolonged air drying, non-cavitated caries lesion.		 RA1
2 Distinct visual change in enamel	Carious opacity, the clinical change must be constant whether the tooth is viewed dry or wet, non-cavitated caries lesion.		 RA2
3 Localized enamel breakdown	There is visible enamel breakdown, The WHO probe can be lightly stroked along a tooth's surface to confirm a cavity that appears to be in the enamel, the dentin is not visible.		

ICDAS Code	Description	Clinical appearances	Radiographic appearances
<p>4</p> <p>Underlying dark shadow from dentin with or without localized enamel breakdown</p>	<p>A shadow of discolored dentin is visible through an apparently intact enamel surface. The darkened area may appear colored in gray, blue, or brown.</p>		
<p>5</p> <p>Distinct cavity with visible dentin</p>	<p>Cavitated lesions are exposing the dentin.</p>		
<p>6</p> <p>Extensive distinct cavity with visible dentin</p>	<p>A large cavity involves at least half of a tooth's crown.</p>		

Proximal caries detection and assessment

Detection of dental caries in the proximal is invisible and inaccessible. The clinical examination by itself is insufficient to diagnose proximal caries and leads to a misdiagnosis. Additional tools such as tooth separation, transillumination, fluorescence devices, and radiographic examination are utilized to detect proximal caries (22, 34).

Tooth separation is the use of elastomeric separation modules to create a small space between the contact of teeth that provides direct visual access to the two adjacent approximal surfaces. A tiny elastomeric band is placed between the suspicious surfaces and left in place for 2–7 days throughout this procedure. Then, a second visit is required for band removing and carious lesions detecting for any approximate lesions. However, this method causes tooth pain and requires cooperation from the patients (28).

Fibre-optic transillumination (FOTI) is the simplest and non-invasive method to enhance visualization by increasing the contrast between sound structure and carious lesions. The method utilizes high-intensity white light directed perpendicularly to the interproximal surfaces. Visually, transillumination of enamel lesions results in a gray, opaque appearance within the tooth, while within dentin lesions it is illustrated as a brown lesion. The disadvantages of this method are that it requires subjective interpretation and it is unable to be used for caries progression monitoring due to a shortage of data storage (28).

Near-infrared light transillumination (NILT) is a new method that presents the enamel and dentin caries lesions by using near-infrared light. It is helpful in the early enamel detection on proximal sites, but their ability reduces in the visualization of the dentin lesion. Therefore, it is difficult to distinguish the caries extension to the dental pulp (28).

The quantitative light-induced fluorescence (QLF) device can detect micro-changes and measure mineral content on the tooth surface. The QLF device's mechanism is based on the different light scattering of fluorescence between demineralized lesions and normal teeth. The QLF device can detect the initial carious lesion, white spot lesion, and matured plaque on the tooth surface by emitting red fluorescence and then showing the result as a fluorescence image. The limitation of this method is its sensitivity to ambient light, which causes difficulty for dimmed room preparation (28).

Laser fluorescence devices such as the DIAGNOdent device are designed for proximal cavity detection, especially at the initial stage of lesions. In conditions where the occlusal and proximal surfaces are suspect, or where radiography is not available, DIAGNOdent can be used as a second opinion device. DIAGNOdent is useless for secondary caries detection because the composite or amalgam restorations may give false-positive readings (28).

The development of diagnostic instruments, such as laser fluorescence devices, has aided in latent caries detection. No clinical trial showed that fluorescence, laser fluorescence devices, or electrical impedance devices accurately detect latent caries (28).

The drawback of all additional devices is the additional expenses and their low sensitivity in dentin (Table3). Furthermore, the additional devices are technique sensitive that can cause false-positive results. Recently, there has been no clinical trial

report on the accuracy of these additional devices in detecting hidden caries, especially secondary caries. Consequently, they are rarely used for proximal caries detection (28).

Table 3 The additional devices and their high sensitivity values in enamel and dentin. (22, 28, 34, 35)

Devices	Sensitivity		Specificity	
	Enamel	Dentin	Enamel	Dentin
Tooth separation	75%	43%	88%	93%
Fibre-Optic Transillumination (FOTI)	70%	57%	87%	93%
Near-Infrared Light Transillumination (NILT)	99.2%	21.9-82%	41.7%	98%
Quantitative Light-Induced Fluorescence (QLF)	71%	64%	84%	88%
Laser fluorescence device	58-97%	67-97%	60-85%	70-87%

A radiographic examination is commonly utilized for caries detection. Before using radiographic imaging in dental procedures, it is critical to have a clear understanding of the basic knowledge of radiology.

Radiation physics and biology

X-rays have been used in dentistry as a necessary part of the dentist's diagnostic tool for a long time. The x-ray beam passes through a patient's face, interacts with hard and soft tissues, and strikes a digital sensor or film in dental and maxillofacial imaging. That is, the intensity of the beam remains constant as it moves out of the center. As the beam passes through the patient, its intensity diminishes, which is referred to as attenuation. This attenuation occurs as a result of individual photons in the beam being absorbed by the tissue atoms or photons being scattered out of the beam. Photons interact with tissue atoms and cease to exist in absorption interactions. Photons interact with tissue atoms through scattering interactions, although they always travel in different directions. These interactions occur at varying rates depending on the type of tissue exposed. Additionally, a few photons penetrate directly through the patient's tissues and reach the sensor, forming a radiographic image (36).

The biological effects of diagnostic and therapeutic radiation are caused by ionizing radiation, which is the interaction of x-ray photons with patient tissue,

resulting in chemical changes within the cell. Radiation damages biological tissue and occurs through direct and indirect actions. In direct actions, the photon directly interacts with the critical areas within the cell, such as the DNA of the cell. The unstable free radicals produced by the ionization interaction cause direct injury by altering biologic molecules from the original molecules, resulting in a biologic change in the irradiated organism. In indirect actions, photons interact with water molecules within the cell, and the free radicals of water ionizations cause biological damage. Radiation damage regardless of direct or indirect actions can be repaired enzymatically within minutes to hours. However, when exposed to a high radiation dose or long-time exposure, the repair mechanism becomes insufficient to repair the tissue injury, resulting in tissue or organ dysfunction (36, 37).

Radiation-induced biologic effects can be classified into two categories. The first one is a deterministic effect caused by cell death that occurs when the radiation dose exceeds a certain threshold, and the severity of the effect increases as the exposure dose increases. Examples of deterministic effects include skin burns, hair fall, cataracts, osteoradionecrosis, and teratogenesis. The second one is a stochastic effect caused by sublethal DNA damage. There is no minimum threshold dose of occurrence. As the dose increases, the probability of the occurrence of the effect also increases. The degree of the effect, on the other hand, is dose independent. Examples of stochastic effects include radiation-induced cancer, tumors, heritable effects, and gene mutation (Figure 10) (36, 37, 38).

Diagnostic radiologic examinations in dental and maxillofacial regions are designed to keep the dose below the threshold dose, which minimizes deterministic effects but may result in stochastic consequences (36).

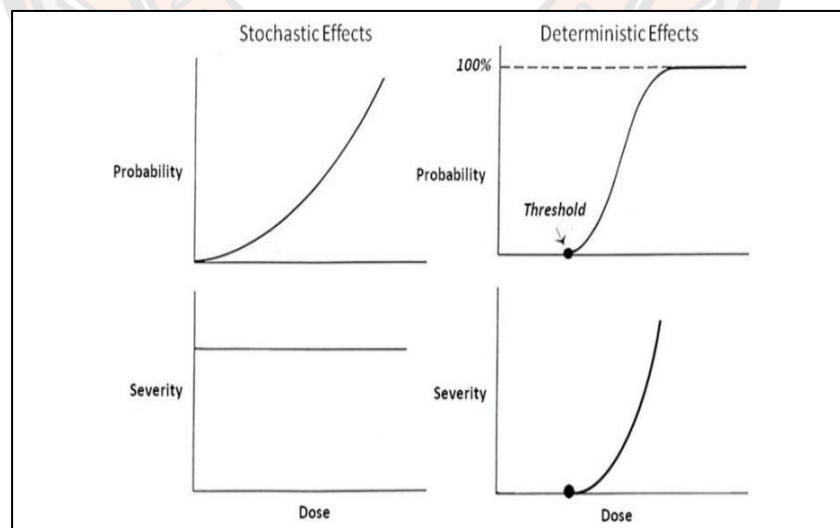


Figure 10 The probability-dose and severity-dose relationships for stochastic and deterministic effects. (38)

Radiosensitivity of Various Organs

A tissue or organ that can be damaged by radiation is called radiosensitive. This includes blood cells, immature cells, and young bone cells, which are radiosensitive. The cell that has rapid cell division is more radiosensitive. On the other hand, cells that are not dividing cells will be low radiosensitive and most radioresistant (36).

The radiosensitivity of an organ is dependent on the radiation dose and the sensitivity of its component cell types is shown in table 4.

Table 4 The relative radiosensitivity of various organs (36)

High	Intermediate	Low
Lymphoid organs Bone marrow Testes Intestines Mucosal lining	Fine vasculature Growing cartilage Growing bone Salivary glands Lungs Kidney Liver	Neurons Muscle

The term "critical organ" refers to an essential organ that has been damaged by radiation and has a detrimental effect on the patient's quality of life. In dental radiographic procedures, the critical organs of the head and neck region include bone marrow, skin, the lens of eyes, and the thyroid gland. Because the position of the thyroid gland is closer to the lower border of the mandible in children than it is in adults, there is a higher risk of radiation exposure. (Figure 12) Therefore, when radiographic examinations of pediatric patients are performed, leaded aprons with thyroid collars should be worn (37, 39).

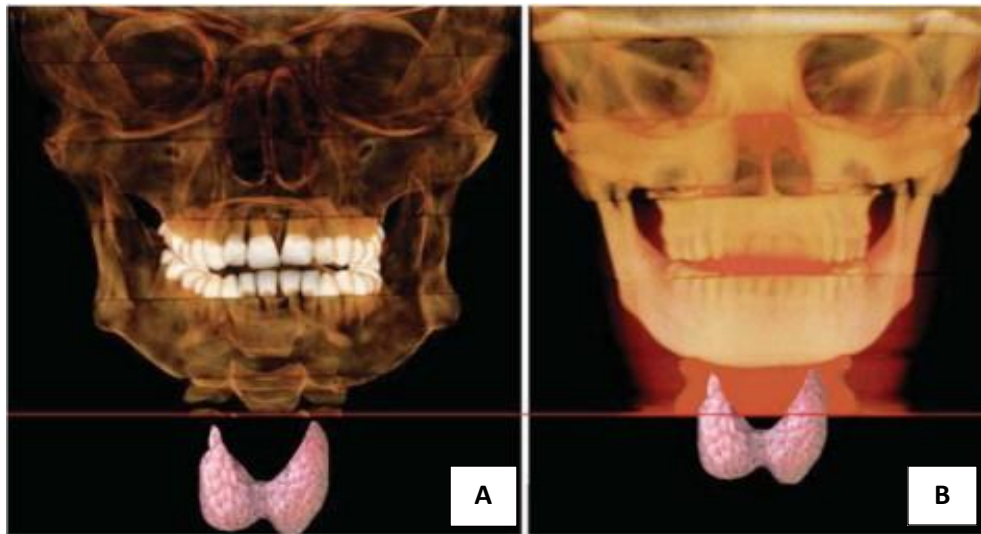


Figure 11 Area of radiation exposure in adult (A) and child (B). (39)

This is obviously significant when considering the adolescent and pediatric populations that routinely receive diagnostic radiation and whose cellular growth and organ development are associated with increased radiosensitivity of tissues. Pediatric patients under the age of 10 years have a threefold increased chance of developing cancer as a result of radiation exposure due to their more radiosensitive tissue and longer lifespan. Therefore, it is important to decide which type of diagnostic imaging is most appropriate for pediatric patients (39, 40, 41).

Radiographic image in dentistry

Dental imaging has a lower exposure dose than medical imaging as in computed tomography (CT). The risk of radiation-induced cancer is low due to the stochastic effect. The total number of dental radiographs, on the other hand, is high. Therefore, the guiding principle in radiation protection must be followed to reduce the radiation dose, especially in pediatric patients. These are three principles: justification, optimization, and dose limitation. Additionally, the principle of ALARA (As Low As Reasonably Achievable) is that the exposure of radiation should be kept to a minimum to protect both patients and dentists from radiation damage. Recently, an update principle for the use of radiographic imaging for diagnostic purposes was published, stating that the exposure dose should be kept as low as diagnostically acceptable (ALADA) (36, 37, 42).

Nowadays, a radiological examination is used in addition to routine clinical examination as a means of detecting dental caries, particularly proximal caries, that are invisible during clinical examination and may result in misdiagnosis. Bitewing radiography is the most commonly used radiographic technique for detecting proximal surface caries (3, 4, 5, 6, 43).

Staging coronal caries lesions radiographically

Radiographic information significantly increases clinical findings in terms of detecting lesions at various stages of progression. The proximal lesions can be scored according to the depth of caries in enamel and dentin using a variety of scoring systems.

The International Caries Classification and Management System (ICCMS™) is a health-oriented system that aims to maintain oral health and dental function. The ICCMS™ approach to caries staging is based on the evidence based ICDAS system. It also takes into account the ICDAS "wardrobe" flexible approach, which allows various options to classify the disease according to local or individual needs, preferences and conditions. The goal of ICCMS™ is to transform understanding of the pathogenesis, prevention, and management of dental caries in a comprehensive way through a complete evaluation and individualized caries treatment plan.

The radiographic staging of caries lesions on posterior teeth during the caries diagnostic procedure, as shown in Table 5. Radiographically, the ICCMS™ classifies posterior tooth surfaces. This grading system's reliability and accuracy have been reported to be of substantial to excellent quality. The radiographic penetration depth at which it may be reliably predicted that the tooth surface is cavitated is in the region of radiolucency deeper than the outer third of dentine. This corresponds to the ICCMSTM radiographic scoring system's scores of 4, 5 and 6 (44).

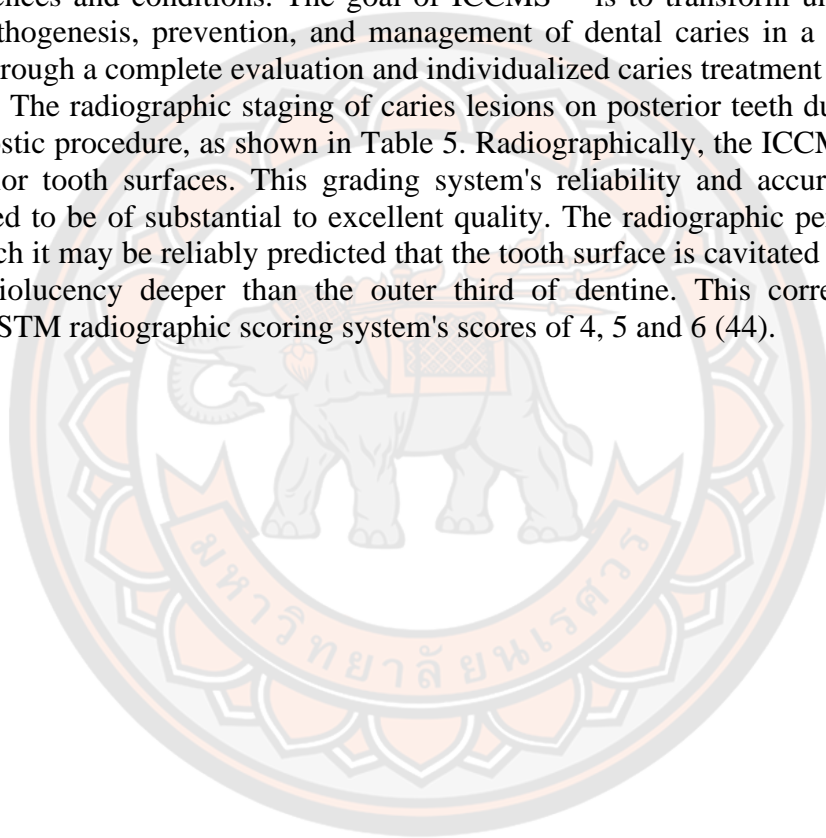
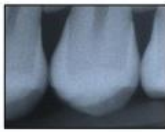
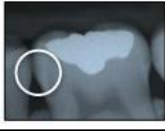

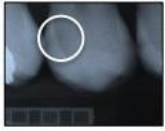


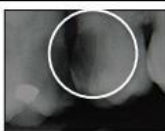


Table 5 ICDAS/ICCMS™ radiographic scoring system. (44)

ICDAS Radiographic scoring system				
ICCMS™ Caries Categories	0	No radiolucency		No radiolucency
	RA: Initial stages	RA 1		Radiolucency in the outer ½ of the enamel
		RA 2		Radiolucency in the inner ½ of the enamel ± EDJ (enamel-dentin junction)
		RA 3		Radiolucency limited to the outer 1/3 of dentin
	RB: Moderate stages	RB 4		Radiolucency reaching the middle 1/3 of dentin
	RC: Extensive stages	RC 5		Radiolucency reaching the inner 1/3 of dentin, clinically cavitated
		RC 6		Radiolucency into the pulp, clinically cavitated

Intraoral bitewing radiograph for proximal caries detection

A precise and appropriate diagnosis of a proximal caries lesion enables rapid operative treatment, thereby avoiding substantial tooth loss. Intraoral bitewings, in particular, have been the most widely used tool for detecting proximal surface caries that are not clinically visible and are often recognized globally for detecting proximal caries. Intraoral bitewing radiographs images capture an image of the crowns of the maxillary and mandibular teeth from the canine's distal surface to the most posterior erupted molar's distal surface as well as the alveolar crest. To obtain an intraoral bitewing image without overlapping contact, patients must be positioned upright in the dental chair, and the posture of the patient's head is critical (3, 5, 6, 36, 43, 45, 46).

Bitewing radiography is approximately 20–30% sensitive for early caries lesions that extend into the outer half of enamel and may be missed diagnostically. The sensitivity increases to 40–60% for more advanced caries lesions or cavitated lesions into the dentin, which are seen on both radiography and clinical examination (28).

Intraoral bitewing films have various limitations, which can be classified into 3 categories: first, patient factors impose constraints such as discomfort and suffering induced by the film or film holder, which results in uncooperative behavior. Children with fear and anxiety who are prone to be a lacking cooperative patient may refuse to bite on the bite tab or snap-a-ray, resulting in loss of the interesting area and inability to diagnose. Furthermore, the pediatric patient's unpredictable movements may result in hazy photos (Figure 12) (36, 42).

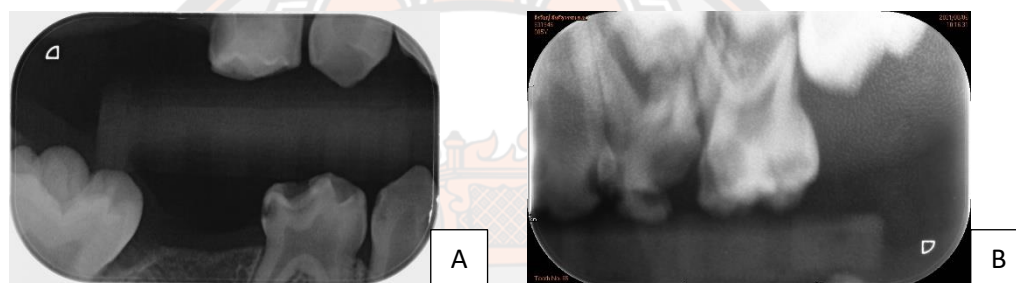


Figure 12 The error from the patient (By the author)

- A: loss of interest area on upper teeth due to patients' refusal to bite on the snap-a-ray.
 B: blurred image caused by patient movement during exposure.

Second, limitations imposed by technical errors depend on the skill level of the operator. Technical errors can occur at any step, for example, the incorrect horizontal angulation of the X-ray tube results in overlapping of the contact surfaces, which is the major drawback of intraoral bitewing radiography. Incorrect vertical angulation of the X-ray tube creates distorted images as well as elongation and foreshortening. The position of the x-ray tube may cause a part of the film to be missed, and incorrect film placement results in cone-cut images and loss of the interesting area. The technical error, whether caused by the patient or the operator, must be corrected by radiographic retakes which increase the patient's radiation exposure and increase the risk of radiation damage (Figure 13) (36, 42).

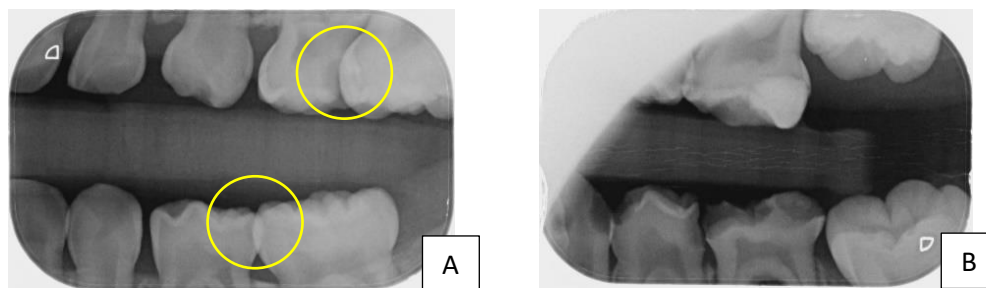


Figure 13 The error resulting from the intraoral bitewing radiography method. (By the author)

A: overlapping of the proximal surface image.

B: cone cut image

Finally, the most relevant to the current situation, Coronavirus disease (COVID-19), is a viral infectious disease caused by the SARS-CoV-2 virus. It spreads through infected fluids such as saliva and respiratory secretions or droplets, which are released when a diseased person coughs, sneezes, or speaks. To contribute to the management of COVID-19 transmission, the dental practice should be changed. Intraoral radiography is one of the dental procedures that generate aerosol from coughing, vomiting, or crying when getting the film and film holder into the uncooperative patient's mouth (7, 8, 9).

Intraoral radiography stimulates the gag reflex in patients with sensitive tissue; a study of gagging in dental radiography discovered that the overall frequency of gag reflex during intraoral radiography was 13%. The frequency of gag reflex differed significantly between trained radiographers (frequency of 9%) and dental students (frequency of 26%) (8, 47).

The ADA has provided interim guidance on minimizing COVID-19 transmission risk for dental health care personnel (DHCPs), recommending the avoidance or reduction of intraoral radiography. Furthermore, oral and maxillofacial radiology provided the guidelines for oral and maxillofacial imaging: COVID-19 considerations to decide on patient management. They recommend using extraoral radiography such as CBCT, panoramic radiography, and extraoral bitewing radiography as an alternative technique to intraoral radiography during this situation (Figure 14) (8).

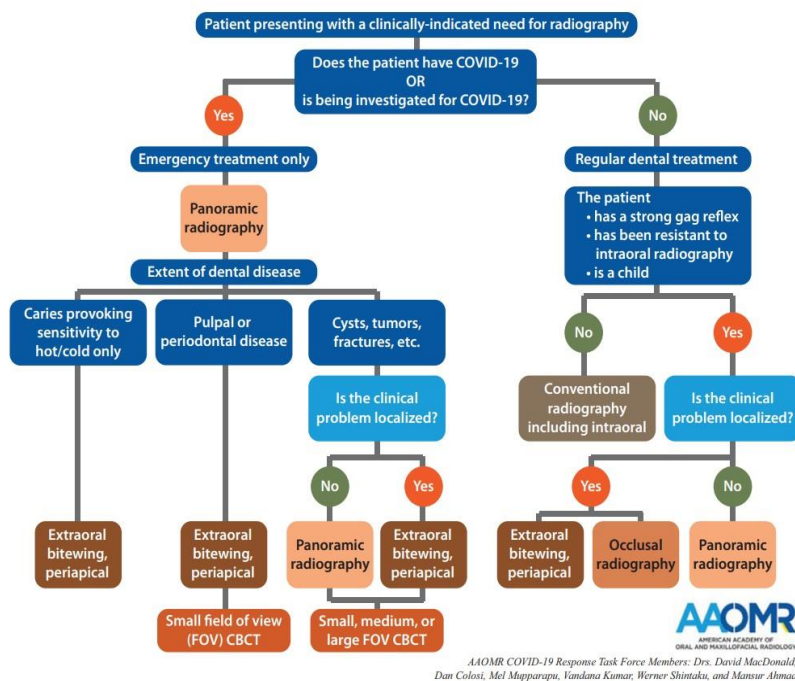


Figure 14 Flowchart for decision making in managing patients in the COVID-19 situation (8)

Extraoral radiograph for proximal caries detection

Extraoral radiography can be used effectively in pediatric dentistry to diagnose a variety of dental conditions. Understanding the techniques and their limitations is crucial when deciding how to obtain the best diagnostic image possible for a pediatric patient. This technique is produced by keeping both the X-ray source and the image detector (image receptor) stationary or by synchronized movement of the image detector and the X-ray source in opposite directions. Interproximal caries are detected using a variety of techniques, including oblique lateral radiographs, CBCT imaging, panoramic imaging, and extraoral bitewing imaging (3, 36).

Oblique lateral radiography for proximal caries detection

Prior to the development of panoramic radiography, extraoral radiography routinely used oblique lateral radiography in. Their popularity has faded away in recent years, and they are now used as an alternative radiographic technique when intraoral radiography is unavailable. The cassette position, the patient's head position and the x-ray tubehead position must be all accurate, which requires experienced operators and cooperative patients (3, 42).

Cone beam computed tomography (CBCT) for proximal caries detection

Cone beam computed tomography (CBCT) is the most significant technological advancement in maxillofacial imaging. They produce a 3D image that is visualized and can be analyzed in three planes: sagittal, coronal, and axial. CBCT

imaging should be used as an adjunctive diagnostic tool for specific indications, not as a screening procedure. CBCT imaging can be used in pediatric patients who have cleft lip and palate for surgical treatment planning, in case of complications, or when conventional imaging is insufficient. The limitations of CBCT are that it causes image artifacts generated by metallic objects such as metallic restorations or stainless-steel crowns (SSC) which are unable to detect caries. Another limitation is the high radiation dose of CBCT imaging. It is essential to protect pediatric patients from radiation exposure by wearing a leaded apron and thyroid. Thus, CBCT imaging for detecting dental caries is used only when the CBCT image is being used for another main purpose (3, 36).

Panoramic radiography for proximal caries detection

Panoramic images are a valuable diagnostic tool where an overview of the jaws is required for initial evaluation. The image detector and the X-ray source move in opposite directions within the synchronized motion. Patient positioning is critical for optimal image quality, which requires strict adherence to the manufacturer's instructions. The tissue within the focal trough is sharply defined in focus while the tissue on the outside is blurred in the image. Panoramic images contain ghost images that are blurred, and significantly magnified, and superimposed on the real image on the opposite side of their true anatomic location. Consider that the dose of radiation is higher than that of intraoral radiography. The major disadvantage of panoramic radiography is that it does not provide the fine anatomic detail that intraoral periapical radiographs do. Thus, it is less effective at detecting small carious lesions (3, 36).

Extraoral bitewing radiograph for proximal caries detection

In the last decade, concepts for panoramic x-ray units that generate extraoral bitewing (EOBW) programs have been developed by use of digital sensors, specialized software, and robotic motion, which is the complex and special movement of a panoramic x-ray tubehead and image receptor, resulting in contacts that are not overlapped (5, 10, 11, 43).

The imaging principle is identical to that of conventional panoramic radiography, in which three stationary centers of rotation are used to create three separate circular arches (Figure 15). The modified rotation movement is achieved by reducing the rotational arc of the x-ray movement in order to decrease the size of the focal trough, thereby reducing patient radiation exposure. They enable rotational maxillofacial radiography to be performed in a flexible, precise, and complex manner. Additionally, the projection angle of the x-ray beam is also modified by improving interproximal angulation projection geometry to ensure that X-ray beam is perpendicular to each contact interface to minimize tooth overlap and superimposition of structures on the opposite side of the jaw (36, 42).

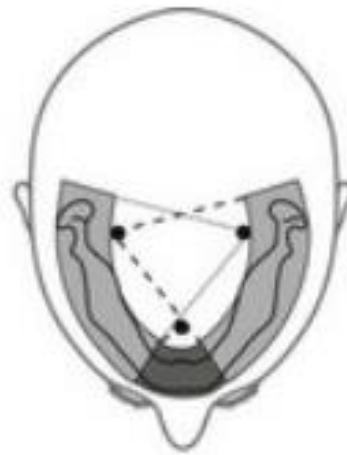


Figure 15 The three stationary centers of rotation in extraoral bitewing radiography (42)

EOBW could be comparable to intraoral bitewing in detecting proximal caries. They produce bitewing-like images of the posterior area, which includes part of the maxilla and mandible, as well as the crown and root structure and alveolar crest bone visible on extraoral bitewing radiography that reveal more information than intraoral bitewings (5, 6, 9, 10, 11) (Figure 16). To obtain the optimal image quality, it is necessary to position the patient according to the manufacturer's instructions (Figure 17) (3). Extraoral bitewing is superior to intraoral bitewing because it captures both the left and right posterior teeth in a single radiation exposure. This represents an improvement over the four intraoral bitewing images (12). As a result, EOBW would be beneficial for pediatric patients who are unable to perform or resistant to intraoral radiography, such as those who are prone to be an uncooperative behavior, have learning or cognitive disabilities, a handicapped or special needs child, have a severe gag reflex, or have anatomical limitations such as large torus mandibularis and torus palatinus (5, 13, 36, 43).

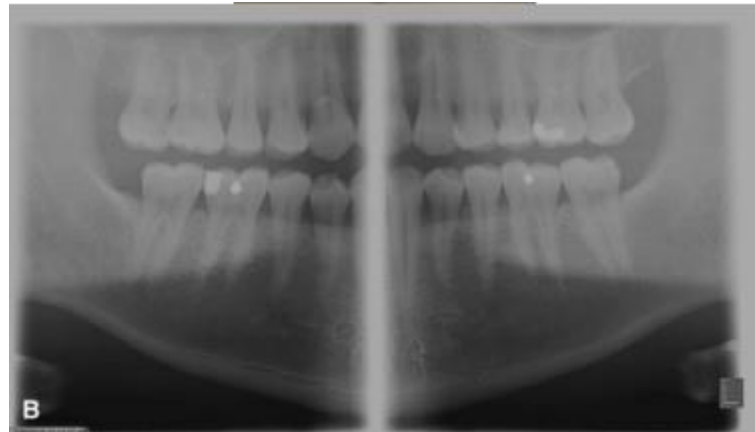


Figure 16 Extraoral bitewings image (36)



Figure 17 The patient's position during the imaging
In a short or a small child, a step footstool can be used to position the patient. (3)

Extraoral bitewing radiographs are recommended as an alternative to intraoral bitewings radiographs to reduce the risk of SARS-CoV-2 transmission and to identify proximal caries for children and adults who struggle to tolerate intraoral radiographs. It would help to improve diagnostic information and the patient's experience during and after this situation. The guidelines for oral and maxillofacial imaging: COVID-19 considerations are shown in Figure 14 (7, 8, 9).

Several *in vivo* and *in vitro* studies compared extraoral bitewing radiography to other modalities such as intraoral bitewing radiography, panoramic radiography, and CBCT to determine the diagnostic accuracy of proximal caries detection in permanent teeth (5, 6, 10, 11, 13, 43).

The *in vitro* studies used different sample preparation techniques and radiographic machines. The extracted human teeth are embedded in the dry human skulls and mandibles during sample preparation (5, 13, 43), whereas Felemban et al used 106 teeth from seven preserved cadaver heads. Regarding the x-ray machine, Abu El-Ela et al. obtained their radiographs using a Sirona digital panoramic X-ray unit (Sirona Siemens, Bensheim, Germany) (13). In other studies, the radiograph images were acquired using a Planmeca Promax Digital Panoramic X-ray unit (Planmeca Inc., Helsinki, Finland) (5, 6, 10, 11, 43).

The results of the extraoral bitewing diagnostic accuracy study are still inconclusive. Kamburoglu et al. conducted an *in vitro* study to compare extraoral bitewing, intraoral bitewing, and panoramic radiography for detection of proximal caries. They concluded that extraoral bitewings and panoramic imaging were less accurate at diagnosing interproximal caries than intraoral bitewings (43). On the other hand, Abdinian et al. showed that extraoral bitewing radiographs were superior to conventional panoramic radiography in detecting proximal caries and the diagnostic accuracy of extraoral bitewing and intraoral bitewing techniques was comparable (5). Similar to the findings of Abu El-Ela et al., they investigated the diagnostic accuracy of intraoral and extraoral bitewing radiography in detecting enamel proximal caries and revealed no differences (13). Additionally, Felemban et al. evaluated the diagnostic accuracy of intraoral bitewings, extraoral bitewings, panoramic radiography, and CBCT, concluding that CBCT and extraoral bitewings could be comparable to intraoral bitewings in detecting interproximal caries (11).

Terry et al. an *in vivo* study on 20 patients and revealed that there was no difference between extraoral and intraoral radiography for detecting proximal caries (6). Chan et al., on the other hand, recruited 116 patients to compare the accuracy of proximal caries and bone loss diagnosis and found that extraoral bitewing was statistically significantly effective in detecting proximal caries and alveolar bone loss. However, false-positive diagnose occurred more frequently than intraoral bitewings (10).

Abu El-Ela et al. (13) conducted their study using a histological examination regarded as the best for grading proximal caries. The limitations of grading the radiological assessment in the previous study was a nominal scale rating from definitely not present caries to present caries. In statistical analysis, the nominal scale is the lowest level of measurement. Furthermore, the thickness of tooth section, which impacts the quality of histological image, was not indicated.

As previously stated, the study regarding the accuracy of extraoral bitewing radiography in detecting proximal caries of primary teeth is ongoing. An application of the extraoral bitewing to identify dental caries in different tooth morphology, especially in primary dentition, is a great challenge. Therefore, we intend to investigate the accuracy of the extraoral bitewing in dental caries detection in primary molars and compare it with histopathological examination utilizing the gold standard.

8. Research Methodology

This experimental research was approved by the Naresuan University Institutional Review Board (IRB No. P1-0076/2565) before it began at the Dental Hospital, Faculty of Dentistry, Naresuan University. The requirement for research conduction in the Dental Hospital and laboratory conduction in, Faculty of Dentistry, Naresuan University, were permitted.

8.1 Population and Sample selection

8.1.1. Population

From October 2021 to October 2022, the extracted posterior primary molars are gathered from the pediatric patients in the Dental Hospital, Faculty of Dentistry, Naresuan University and private dental clinics in Phitsanulok, Thailand.

8.1.2. Sample selection

The first and second primary molar are extracted due to pathologic root resorption, with or without dental caries, or infection indicated.

The sample size is calculated at 85% power of test and 95% level of confidence by using G*power program version 3.1.9.7 (Franz Faul, University Kiel, Germany). A total of 56 primary molars were used in this study, representing 112 surfaces.

8.2 Inclusion Criteria

The first or second primary molar with pathologic root resorption, with or without dental cavities or infection.

8.3 Exclusion Criteria

8.3.1 The first or second primary molar with large dental cavities on buccal or lingual surface or extensive proximal caries extending to the buccal, lingual or root surfaces. These would be difficult to evaluate radiographically due to the superimposition of images.

8.3.2 The first or second primary molar with restoration on proximal surface or stainless-steel crown (SSC).

8.3.3 The first or second primary molar which has abnormal development or structure such as hypomineralized teeth, amelogenesis imperfecta, dentinogenesis imperfecta, enamel hypoplasia, dentin dysplasia, crack teeth, fracture teeth or any abnormality caused a difficulty in radiographic interpretation.

8.4 Variables in the research

8.4.1 independent variable: Extraoral bitewing radiography

8.4.2 dependent variable: The accuracy of the proximal caries detection in primary molar.

8.5 Data collection

Sample preparation and grouping

The primary molars were debris-free and preserved in 0.1% thymol solution at standard ambient temperature as 25 °C. Then, all teeth were split into crown and root sections using hi-speed diamond bur under water irrigating. Fifty-six teeth were randomly assigned an identity number and divided into seven groups, which consisted of four upper primary molars and four lower primary molars in each group.

Each group of teeth was set up in the mimetic alveolar sockets of 3D printed-skull and mandible models, made from polylactic acid (PLA) to simulate the position of posterior teeth in the oral cavity. The teeth of each group were occluded and fixed by dental baseplate wax to cover the cemento-enamel junction (CEJ) of the crown. A 3D-printed model was made from a CBCT image of a 7-year-old male patient, taken for orthodontic reasons, in which all primary molars on the CBCT images were deleted and attuned to the model with the Meshmixer™ program version 3.5.474 (Autodesk, California, USA, Inc.).

Calibration

The inter- and intra-examiner calibration for radiographic images and histological images was evaluated using weighted kappa coefficients. The Kappa statistics was calculated according to the following criteria: < 0.20, poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.00, excellent agreement. The intra- and inter-examiner calibration must be rated as excellent, with a weighted kappa coefficient greater than 0.80. When the inter-observer agreement was less than 0.8, the observer must repeat the process until an excellent result was obtained. Besides this, if two observers disagree, a consensus was reached through discussion with a third observer. Additionally, all teeth which had been used in the calibration process were excluded from this study.

Radiographic calibration

Prior to radiographic evaluation, the examiner must pass a radiographic calibration with one dental radiologist. The examiner evaluated 3 extraoral bitewing images and 6 intraoral bitewing images, representing 48 proximal surfaces in each modality. After one week of radiographic imaging preparation, eight primary molars with sound and various levels of proximal caries were used in calibration. For inter-examiner calibration, all radiographic images were evaluated independently and in random order. Each image was displayed on the same computer monitor (21 inch-high-definition light-emitting diode screen; OptiPlex 3050, Dell®, Round Rock, Texas, USA) using the Uniweb server program under the ambient lightroom. To improve radiography examination, each examiner can freely adjust the brightness and contrast tools. For intra-examiner calibration, the examiner evaluated separately twice at one-week intervals to minimize the possibility of recalling previous decisions.

Histological calibration

After completing the radiographic calibration, the examiner randomly selected primary molars that were used for radiographic calibration to section at a thickness of 0.5 mm. by using a macrotome (Isomet 5000; Buehler, Lake Bluff, IL, USA). There were 10 slices in total. Each slice was evaluated on both front and back sides of the slice and on both proximal surfaces of the tooth. Therefore, 20 images of ground section, representing 40 proximal surfaces (both mesial and distal surfaces), were used for calibration.

Prior histological evaluation, the examiner must be passed calibration with one pathologist. The examiner evaluated all ground sections under the stereomicroscope (Olympus SZX16, Hatagaya, Shibuya-ku, Tokyo, Japan) at x 12.5 magnification, which can display both mesial and distal surfaces in the histological image, based on pilot studies. The calibration began after one week of completing all histological sections to minimize the possibility of remembering images. For inter-examiner calibration, all histological images were evaluated independently and in random order. Each image was displayed on the same computer monitor (23-inch light-emitting diode backlight screen; Pavilion23fi, HP®, Palo Alto, California, USA) using the Olympus cellSens software program under the ambient lightroom. To improve image quality, the examiner can freely adjust the coarse and fine focusing knob on each ground section. For intra-examiner calibration, the examiner evaluated separately twice at one-week intervals to minimize the possibility of recalling previous decisions.

Image acquisition

1. Acquisition of intraoral bitewing

Intraoral bitewing was acquired on both proximal surfaces of primary molars using the Dixelmega™ (J. Morita Mfg. Corp., Kyoto, Japan) and photostimulable phosphor (PSP) plates size #0. The exposure factor was adjusted according to the child patient mode of instruction manual setting at 60 kV, 7 mA, and 0.20 s with a focus-receptor distance of 30 cm. (43) The intraoral bitewing radiographs using the paralleling technique were performed with a positioning indicator device (RINN XCP-PSP fit®, DentSply Sirona, Pennsylvania, New York, USA). The receptor should be parallel to the long axis of the teeth. The anterior border of the receptor should extend beyond the contact area between the primary mandibular canine of 3D model and the first primary molar. The X-ray tube was parallel to the positioning indicator device in the vertical angulation, and the beam was directed through the interproximal surface of the primary molar in the horizontal angulation (Figure 18) (36).

2. Acquisition of extraoral bitewing

Extraoral bitewing was acquired on both proximal surfaces of primary molars using the Veraview X800™, (J. Morita Mfg. Corp., Kyoto, Japan). The exposure factor was adjusted according to the child patient mode of the instruction manual setting at 80 kVp, 6 mA, and 11.99 s. The models were placed on the chin rest and the position set up to the line of x-ray detector (laser beam). The facial midline of the model lined up with the vertical laser beam, while the horizontal laser beam lined up with the model's orbitale (Figure 19).



Figure 18 Position of the skull and mandible during intraoral bitewing exposing.

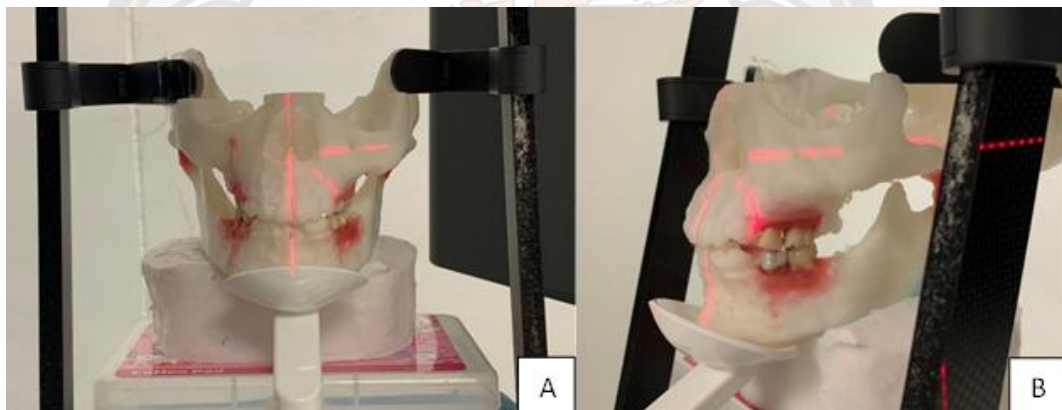


Figure 19 Position of the skull and mandible during extraoral bitewing exposing. (A) coronal view, (B) sagittal view.

Image evaluation

A total of 21 radiographic images, including 7 extraoral bitewing radiographic images and 14 intraoral bitewing radiographic images, were evaluated independently and in random order by two calibrated observers, including a general dentist and a dental radiologist with 8 years of experience. Each image was displayed on the same computer monitor (21 inch-high-definition light-emitting diode screen; OptiPlex 3050, Dell®, Round Rock, Texas, USA) using the Uniweb server program under the ambient lightroom. Each observer evaluated separately twice at one-week intervals to minimize the possibility of recalling previous decisions. The evaluation period was set at 30 minutes, followed by a 15-minute rest period to prevent observer fatigue. To improve radiography interpretation, observers can freely adjust the brightness and contrast tools (Figure20).



Figure 20 Examples of intraoral and extraoral bitewing images, of the same group

Microscopic examination

After completion of radiographic evaluations, all teeth were sectioned for the gold standard test. Determine the center of the lesion and borderline of sectioning by transilluminating a tooth using Mini LED™ (Acteon, Norwich, UK). Then, draw the first line at the location of the deepest lesion, followed by other lines that extend millimeter by millimeter in a bucco-lingual direction from the first line until it completely covers area of the lesion (Figure 21).

Next, the tooth was individually placed in the silicone mold with dimensions of 10 x 15 x 15 millimeters, and then was poured with a clear epoxy resin up to its occlusal surface. After completion of resin hardening, each resin tooth block was fixed on an acrylic sheet of 2 mm thickness and cut into 4-6 sections, depending on the dimension of proximal caries, serially sectioned and mesiodistally parallel to the long axis of the crown by using a diamond blade with a macrotome (Isomet 5000; Buehler, Lake Bluff, IL, USA). The microscopic examination was performed on the deepest lesion from all sections. Each slice has a thickness of 500 μm. (Figure 22-23).

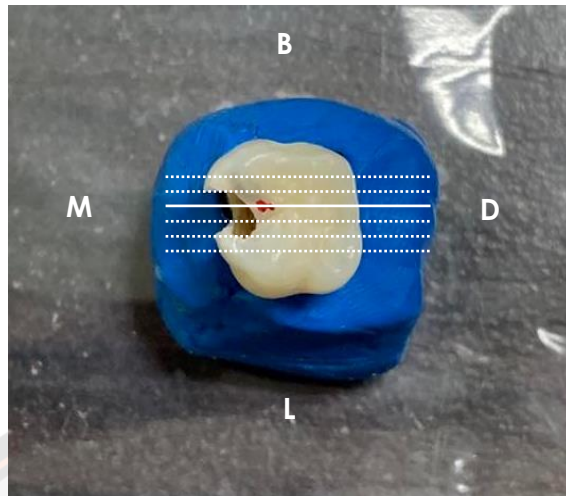


Figure 21 Drawing a line on the sample.
The first line (bold line), and the remaining lines (dash line)



Figure 22 The position of tooth sectioning

After completion of histological sections, 269 slices of histological sections were assessed on both front and back sides of the slice and on both proximal surfaces of the tooth (Figure 24). In total, 538 histological images were evaluated proximal caries under the stereomicroscope (Olympus SZX16, Hatagaya, Shibuya-ku, Tokyo, Japan) at x 12.5 magnification, which is based on pilot studies to ensure optimal image quality.



Figure 23 Each tooth was cut into 4-6 sections depending on the dimension of proximal caries.

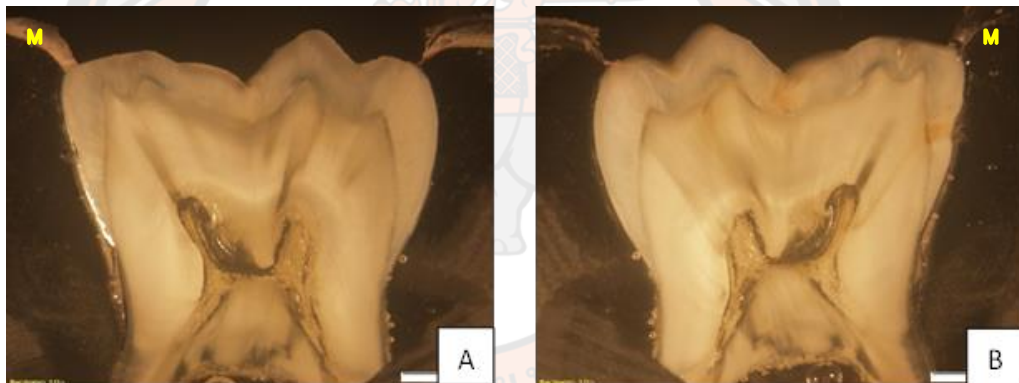


Figure 24 Both front (A) and back (B) sides of slice

Evaluation period was set at 30 minutes per session, followed by a 15-minute rest to prevent observer fatigue under the ambient lightroom. The evaluation was repeated twice at one-week intervals to reduce the possibility of the observer recalling previous decisions. The criterion for enamel caries is an opaque-white to dark-brown discoloration (Figure 25). In the part of the dentin that was examined at the upper border of the sclerosis dentin layer, which was a dark yellow or brownish discoloration (Figure 26) (26, 27). In the case of histological evaluation, if there was a discrepancy between the first reading and the second reading, the pathologist resolved the discrepancy.

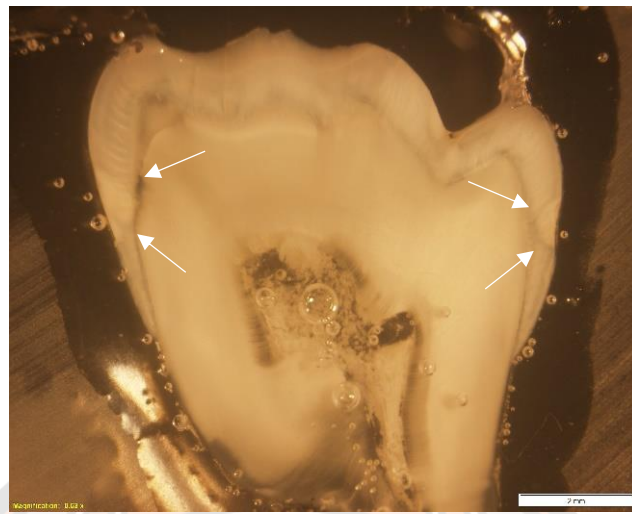


Figure 25 Histological ground section of the proximal enamel caries

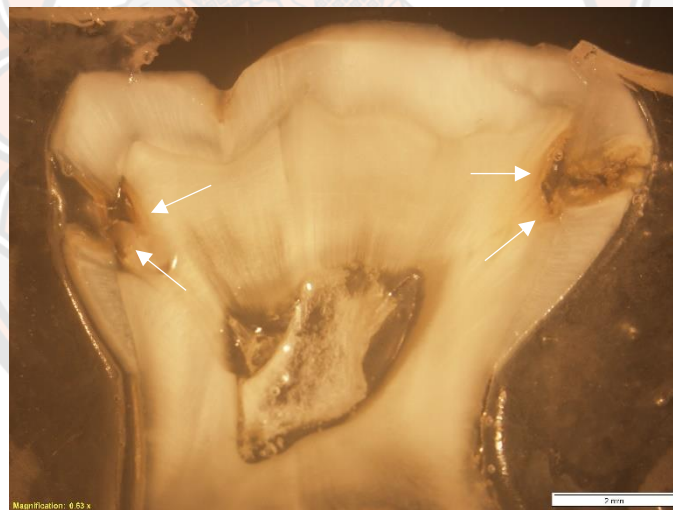


Figure 26 Histological ground section shows the proximal caries at the dentin layer (arrow).

8.6 Data assessment

The radiographic evaluations were scored using a five-point scale (0-4) according to the criteria given by Russell and Pitts (48) as follows: 0 indicates no radiolucency visible; 1 indicates radiolucency area deep to the outer half of enamel; 2 indicates radiolucency area deep to the inner half of enamel; 3 indicates radiolucency area deep to the outer half of dentine; and 4 indicates radiolucency area deep to the inner half of dentine. If there is interproximal overlap at the contact area on the radiographic image, it was not evaluated or rated.

The histological evaluations were scored using a five-point scale (0-4) as follows: 0 indicates no proximal caries; 1 indicates proximal caries in the outer half of the enamel; 2 indicates proximal caries in the inner half of the enamel; 3 indicates proximal caries in the outer half of the dentine; and 4 indicates proximal caries in the inner half of the dentine.

8.7 Data analysis

All data were compared and statistically analyzed using IBM SPSS v. 26 (IBM Corp., 26.0 (IBM Corp., New York, NY; SPSS Inc., Chicago, IL, USA)).

A descriptive statistic was used to describe the distribution and frequency of sample size.

The inter- and intra-observer agreements for radiographic images were evaluated using weighted kappa coefficients. The Kappa statistics was calculated according to the following criteria: < 0.20, poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.00, excellent agreement.

The Mann-Whitney U test was used to determine whether there was a statistically significant difference between the radiography grading scores of each imaging modality and the gold standard histological examination grading scores of each surface.

The Wilcoxon signed-rank test was used to determine whether there was a significant difference between the caries grading scores obtained by the two imaging modalities.

The receiver operating characteristic (ROC) analysis was used to evaluate observers' ability to differentiate between teeth with varying degrees of dental caries. Area under the curve (AUC) ROC mean values from two observers and the overall mean value are calculated to determine the diagnostic performance of two imaging modalities. The following criteria was used to interpret the AUC_{ROC} values: < 0.50 indicates no diagnostic value; 0.50–0.75 indicates a poor diagnostic value; 0.75–0.90 indicates a good diagnostic value; > 0.9 indicates an excellent diagnostic value (49). Additionally, diagnostic accuracy was calculated by comparing the radiographic scores of each imaging modality to the gold standard. This includes sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) (5).

9. Result

Fifty-six primary molars, which represented 112 surfaces, were included in this study. In total, 21 surfaces were sound, and 91 surfaces were carious lesions, which were 24 surfaces of non-cavitated caries and 67 surfaces of cavitated caries.

The proximal surfaces that overlapped by more than half of the enamel thickness of another tooth were excluded from the statistical analysis. There were a total of 92 surfaces for extraoral bitewing images (17.8% overlapped surfaces) and 106 surfaces for intraoral technique (5.4% overlapped surfaces).

Table 6 shows the descriptive data and frequency of sample size for extra- and intraoral bitewing after excluding the overlapped surfaces. Tables 7-8 show the frequency of carious lesions for each modality, which was confirmed by the histological examinations.

Table 6 The frequency and percentage of the radiographic modalities after excluding the overlapped surfaces.

Radiographic modalities	Sound surface (%)	Carious lesions		Total (%)
		Non-cavitated lesions (%)	Cavitated lesions (%)	
IOBW	20 (18.90)	23 (21.70)	63 (59.40)	106 (100.00)
EOBW	19 (20.70)	21 (22.80)	52 (56.50)	92 (100.00)

IOBW, intraoral bitewing; EOBW, extraoral bitewing

Table 7 The frequency and percentage of classified depth of carious lesions in the intraoral bitewing images.

Depth of caries	Carious lesions		Total (%)
	Non-cavitated (%)	Cavitated (%)	
1/2 outer of enamel	7 (8.10)	-	7 (8.10)
1/2 inner of enamel	12 (13.90)	5 (5.90)	17 (19.80)
1/2 outer of dentine	4 (4.70)	15 (17.40)	19 (22.10)
1/2 inner of dentine	-	43 (50.00)	43 (50.00)
Total	23 (26.70)	63 (73.30)	86 (100.00)

Table 8 The frequency and percentage of classified depth of carious lesions in the extraoral bitewing images.

Depth of caries	Carious lesions		Total (%)
	Non-cavitated (%)	Cavitated (%)	
1/2 outer of enamel	6 (8.20)	-	6 (8.20)
1/2 inner of enamel	11 (15.10)	5 (6.80)	16 (21.90)
1/2 outer of dentine	4 (5.40)	15 (20.60)	19 (26.00)
1/2 inner of dentine	-	32 (43.90)	32 (43.90)
Total	21 (28.70)	52 (71.30)	73 (100.00)

The weighted kappa coefficients showed excellent intra- and inter-observer agreements between each radiographic modality and observer in Table 9.

For the non-cavitated group, the Mann-Whitney U test showed a significant difference between the radiographic grading scores of the intraoral bitewing images and the gold standard histological examination ($p = 0.000$) as well as between the extraoral bitewing and histological examination ($p = 0.000$). For the cavitated group, the test showed no significant difference between the caries grading scores obtained by the two imaging modalities in both groups ($p > 0.005$) (Table 10-11).

The Wilcoxon signed-rank test showed no significant difference between the caries grading scores obtained by the two imaging modalities in both groups ($p > 0.005$). The data of statistical analysis were shown in Table 12.

Table 9 Intra- and inter-observer agreements for each observer reading.

Radiographic modalities	Intra-observer agreements		Inter-observer agreements	
	Observer 1	Observer 2	1 st reading	2 nd reading
IOBW	0.954	0.908	0.817	0.803
EOBW	0.843	0.858	0.824	0.812

IOBW, intraoral bitewing; EOBW, extraoral bitewing

Table 10 The differences between the radiographic grading scores of two imaging modalities and the gold standard histological examination in non-cavitated lesions (Mann-Whitney U Test).

Radiographic modalities/Observer	Mean rank	Gold standard	p value
		Mean rank	
IOBW			
Observer1	14.19	28.81	0.000*
Observer2	12.19	30.81	0.000*
EOBW			
Observer1	13.00	30.00	0.000*
Observer2	13.90	29.10	0.000*

IOBW, intraoral bitewing; EOBW, extraoral bitewing

* Statistically significant p-values < 0.05

Table 11 The differences between the radiographic grading scores of two imaging modalities and the gold standard histological examination in cavitated lesions (Mann-Whitney U Test).

Radiographic modalities/Observer	Mean rank	Gold standard	p value
		Mean rank	
IOBW			
Observer1	59.75	67.25	0.173
Observer2	61.67	65.33	0.495
EOBW			
Observer1	52.65	52.35	0.951
Observer2	51.77	53.23	0.773

IOBW, intraoral bitewing; EOBW, extraoral bitewing

Table 12 The differences between the radiographic grading scores of two imaging modalities in both groups of carious lesions (Wilcoxon Signed Ranks Test).

Radiographic modalities/carious lesion	p value
Intraoral bitewing -extraoral bitewing for observer 1	
Non-cavitated caries	0.167
Cavitated caries	0.469
Intraoral bitewing -extraoral bitewing for observer 2	
Non-cavitated caries	0.334
Cavitated caries	0.668

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the area under the ROC curve (Az value) of non-cavitated and cavitated caries for each observer are presented in Table 13. The sensitivity and the area under the ROC curve for cavitated caries were higher for extraoral bitewing, while for non-cavitated caries, they were higher for intraoral bitewing. Figure 27 (A-B) shows the ROC curve of the two observers for non-cavitated and cavitated caries, respectively.

Table 13 The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the area under the ROC curve (Az value) for each radiographic modality for each observer

Radiographic modalities / Dental condition	Observer 1					Observer 2					
	Sensitivity	Specificity	PPV	NPV	Az value	Sensitivity	Specificity	PPV	NPV	Az value	SE
IOBW											
Non-cavitated caries	0.95	0.83	0.51	0.59	0.09	1.00	1.00	1.00	0.50	0.57	0.09
Cavitated caries	0.95	0.98	0.61	0.89	0.04	1.00	1.00	1.00	0.67	0.91	0.04
EOBW											
Non-cavitated caries	1.00	1.00	0.51	0.57	0.09	1.00	1.00	1.00	0.53	0.56	0.09
Cavitated caries	1.00	1.00	0.68	0.91	0.04	1.00	1.00	1.00	0.70	0.92	0.03

PPV, positive predictive value; NPV, negative predictive value; SE, standard error

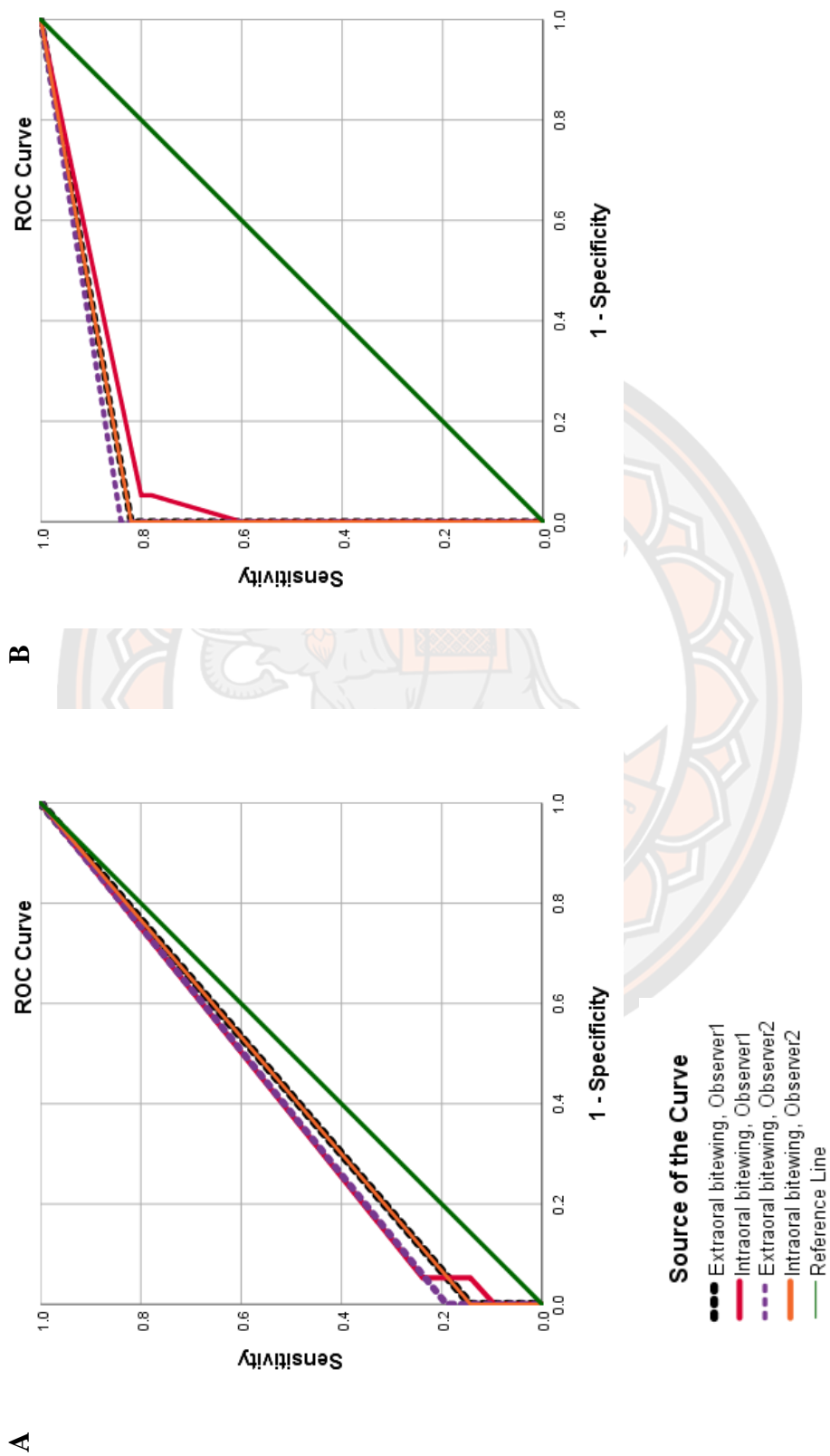


Figure 27 The ROC curve of two observers for detecting (A) Non-cavitated caries (B) Cavitated caries.

10. Discussion

Dental caries, which is one of the most prevalent oral diseases in children, can be diagnosed based on direct visual or visual-tactile examination by detecting the discoloration and discontinuity of the tooth surface. Proximal caries, which occur between the interproximal surfaces of two adjacent teeth, are difficult to detect by only the direct visual method. Therefore, intraoral radiography is an additional method for the detection of proximal caries (15, 43, 50). For children, radiography can provide difficulties. Children's small anatomic structures and potential behavioral issues mean that, while the concepts of periapical radiography are the same as those for adults, in practice, children require specific treatment. Smaller periapical receptors must be used because the dentition and arches are smaller. Further adjustments to receptor placement may be necessary due to the shallow palate and floor of the mouth. Some of the limitations of intraoral radiography might lead pediatric dental patients to become uncooperative (36, 42). In order to overcome these issues, extraoral radiographs were introduced as a new concept called extraoral bitewing (43).

Extraoral bitewing radiograph was produced by certain panoramic radiography machines. These radiographic images show more information than intraoral bitewing because they display the crown and root structures of both left and right posterior teeth within a single radiation exposure. Thus, it would be a benefit for pediatric patients who are not tolerant to intraoral radiographs, have difficulty with intraoral receptor placement, or who have a severe gag reflex (5, 12, 13, 36, 43). These days, the detection of proximal caries can be obtained by extraoral bitewing in the permanent teeth, although it was not a frequent method for primary teeth. Due to the limited knowledge available, we hypothesized that the extraoral bitewing radiograph could reveal proximal caries. The aim of this study was to compare the accuracy of extraoral bitewing for the detection of proximal caries in primary molars, with the gold standard histopathologic examination.

The primary teeth have a different morphology and microstructure when compared to the permanent teeth, such as a smaller size of teeth, a thinner thickness of enamel and dentine, and a lower mineral composition. As a result, the occurrence of dental caries in primary teeth is more rapidly progressive than in permanent teeth (23, 24, 25). This study experimented on primary molars with various depths of caries, whereas other studies utilized permanent premolars and molars (5, 11, 13, 43). The investigations of the extraoral bitewing accuracy were carried out by using human skulls and their mandibles to resemble real dental arches (5, 13, 43), while the heads from cadavers were used in Felemban's study to represent the soft tissue of the face (11). In this study, a 3D-printed skull was constructed from the dataset of CBCT images of a 7-year-old male patient, which simulated the real size of the child's skull and mandible. The primary teeth were arranged in open contacts and set in the sockets along the alignment of the upper and lower dental arches. For evaluating the ability to separate contacts of intra- and extra-oral bitewing, the results presented that twenty tooth surfaces (17.8%) were overlapped for extraoral bitewing and six tooth surfaces (5.4%) for intraoral radiograph. Similar to the clinical study of Terry et al, the proximal overlap of extraoral bitewing was 18.3% and 4.1% of intraoral radiograph (6). In this study, we supposed that there was an inharmonious relation between the

size of teeth and the dental arches because the various sizes of teeth were gathered from many patients, and inappropriate teeth arrangement contributes to improper teeth alignment. The overlapped surfaces on the extraoral bitewing were greater than those found on the intraoral bitewing because of the difficulty in horizontal angulation adjustment for the misaligned teeth, such as from crowding and rotational teeth, from X-ray beam angulation preset by the manufacturers.

A histological examination is regarded as an accurate assessment of the presence of dental caries (13). The result showed excellent intra- and inter-observer kappa coefficients for extra- and intra-oral bitewing. This was in accordance with a previous investigation of Abdinian M. et al., which reported excellent inter- and intra-observer agreement for intraoral bitewing, extraoral bitewing, improved interproximal panoramic, improved orthogonality panoramic, and conventional panoramic radiographs for the detection of proximal caries (5). On the other hand, Kamburoglu et al. and Abu El-Ela et al. showed moderate to strong inter- and intra-observer agreement (13, 43). Kamburoglu et al. reported that intraoral bitewings had higher intra-observer agreement than extraoral bitewings (43). The excellent inter- and intra-observer agreement in this study could reflect the high level of observer experience and ability, as well as the good quality of the calibration and radiograph images between two observers, including a postgraduate dental student in a master's degree program and a dental radiologist with over five years of experience in radiographic examinations.

The division of teeth with carious lesions into cavitated and non-cavitated groups revealed a higher sensitivity of approximately 85% for extraoral bitewing in the cavitated caries and showed high specificity in all groups. In the cavitated group, higher sensitivity, specificity, PPV, and NPV were obtained by extraoral bitewing images followed by intraoral bitewing radiography for both observers in two radiographic modalities. Radiographic imaging is still necessary in the cavitated carious lesions to assess the relationship between caries and dental pulp tissue for proper treatment planning. The results of our study correlated with those of Felemban et al., who found that extraoral bitewings had higher sensitivity than intraoral radiographs. In addition, the restoration on adjacent proximal surfaces affected the accuracy of caries detection. The changes in sensitivity and specificity in two-dimensional images could be related to the superimposition of restoration (11).

An inspection of non-cavitated caries or incipient caries in the primary molars differed from the extraoral bitewing images of the permanent teeth due to their thinner enamel layer (13, 36, 43). Silva Neto JM et al. (51) reported a 6.8% sensitivity of intraoral bitewing for detection of enamel caries, while our results showed 14–19% and 13–22% sensitivity of extra- and intra-oral bitewing, respectively. According to Abu El-Ela et al. 2016 (13), intraoral bitewing had higher sensitivity than extraoral bitewing in the incipient proximal caries detection because of smaller pixel size and better resolution. Even if extraoral bitewing had lower sensitivity than intraoral images in non-cavitated caries detection, there was no significant difference between the radiographic grading scores of both modalities in diagnostic accuracy. Radiographic detection of proximal caries depends on the mineral loss. With at least 40% loss of mineral content in enamel and dentin, a carious lesion has been radiographically visible. Non-cavitated lesions with less than 40% loss of mineral

content, which was undetectable on radiographs, contribute to the underestimated caries extension. Thus, additional clinical examinations such as tooth separation for direct evaluation and the operator's experience are valuable in proximal caries diagnosis (36, 52, 53, 54).

The receiver operating characteristic analysis (ROC) or Az values were used to assess the diagnostic accuracy of the two imaging modalities by comparing the caries grading score by extra- and intra-oral bitewing with the histological gold standard. The Az value for cavitated caries revealed that the diagnostic value of the extraoral bitewing was excellent, similar to the intraoral bitewing. The criteria used to interpret the AUC_{ROC} values are as follows: Ray P. et al., 2010: value < 0.50 indicating no diagnostic value; 0.50–0.75 indicating poor diagnostic value; 0.75–0.90 indicating good diagnostic value; and value > 0.9 indicating excellent diagnostic value (49). We obtained similar Az values to Kamburoglu et al. (43) and Abu El-Ela et al. (13), but a higher Az value than the studies of Terry et al. (6), Abdinian et al. (5), and Felemban et al. (11). The Az values obtained from different caries methods were dependent on the depth of dental caries (11, 43). In our study, 44 of 112 surfaces had deep cavitated carious lesions, which could increase the observer's ability to detect proximal caries. Although the ability of extraoral bitewing radiography in non-cavitated caries detection was lower than in cavitated ones, it was a recommended method for proximal caries diagnosis and oral cavity screening during routine dental checkups when the intraoral bitewing was limited.

The accuracy of proximal caries detection using extraoral bitewing depends on several factors, includes the depth of the caries, the alignment of the teeth, the size and form of the arch, the patient's position, and cooperation (3). The results of the *in vitro* study on the accuracy of proximal caries detection showed a correlation between the caries depth and the ability of proximal caries detection from extraoral bitewings. In the advanced stage of dental caries, the lower mineralized content of tooth structure allows more X-ray photons to penetrate through these regions, creating an obvious radiolucent region on the images. Additionally, appropriate patient preparation and positioning within the focal trough affect extraoral bitewing image quality (36). This study experiment used a 3D-printed model that was unable to simulate the soft tissues of the face. As a result of scattered radiation and the image noise reduction, the proximal caries clearly appear on the images, which enhanced the proximal caries diagnosis (13, 43). Owing to the *in vitro* study, the correlation between the variables associated with patients could not be summarized in this study. Radiography in a child could be a challenging experience, patient management could be performed to decrease dental fear and anxiety and make the patient more comfortable.



The radiosensitivity of an organ depends on the radiation dose and the tissue sensitivity. In children, the critical organs of the head and neck region, such as the thyroid glands, are closer to the lower border of the mandible than they are in adults. Therefore, radiation protection is essential for pediatric patients because children are at a higher risk of radiation exposure. The radiation doses from the radiographic examination must be optimized while producing a diagnostically acceptable image by reducing unnecessary exposure and using protective aprons for the patients (3, 36). Considering the radiation dose, the effective dose is a biological effect measurement of the ionizing radiation, expressed in units of micro-sieverts (μSv). The effective

dose of extraoral bitewing radiographs was 5.82–16.84 μSv (41, 55). The effective dose of panoramic image was a higher effective dose, which was in the range of 17.93–36.0 μSv while intraoral bitewing was 0.3–1.4 μSv (55, 56, 57). Although the extraoral bitewing produced an effective dose three to 11 times higher than the intraoral bitewing, its dose was comparable to 2.5 days of natural exposure (36, 41). The radiograph taken for the patient with mixed dentitions in the first dental visit, 12 intraoral radiographs of full-mouth series, or the intraoral bitewing, combined with panoramic radiography, produced more radiation dose than one extraoral bitewing radiograph. From the results of this study, we suggested that extraoral bitewing could be used instead of multiple radiographic taken to decrease the received radiation dose and increase patient cooperation. Further studies should be experimented with either lower radiation doses or larger sample sizes. The clinical investigation in pediatric patients would confirm the accuracy of extraoral bitewing in proximal caries detection.

In summary, the result of this study was according to the hypothesis that the accuracy of the extraoral bitewing was no different from the gold standard histopathological examination in terms of the detection of cavitated caries on proximal surfaces of primary molars. The precision of caries detection, however, was less than the histopathological examination. The difference in the radiographic grading score of caries between extra- and intra-oral bitewing images was insignificant. Extraoral bitewing could detect cavitated carious lesions on the proximal surfaces of the primary teeth. Therefore, extraoral bitewing radiography could be an alternative tool to conventional bitewings for pediatric patients who were uncooperative or were intolerant to intraoral radiography.

Appendix

This study was approved by the Naresuan University Institutional Review Board (IRB No. P1-0076/2565)

COA No. 0306/2022	AF 11/6.0
IRB No. P1-0076/2565	
 <p>คณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยนเรศวร 99 หมู่ 9 ตำบลท่าโพธิ์ อำเภอเมือง จังหวัดพิษณุโลก 65000 เบอร์โทรศัพท์ 05596 8752</p>	
<p>หนังสือรับรองโครงการวิจัยครั้งแรก</p> <p>คณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยนเรศวร ดำเนินการให้การรับรองโครงการวิจัยตามแนวทางหลักจริยธรรมการวิจัยในคนที่เป็นมาตรฐานสากล ได้แก่ Declaration of Helsinki, The Belmont Report, CIOMS Guideline และ International Conference on Harmonization in Good Clinical Practice หรือ ICH-GCP</p>	
ชื่อโครงการ	: ความแม่นยำของภาพถ่ายรังสีทึบสีกับทึบสีของปากเปรียบเทียบกับภาพพยาธิวิทยาเนื้อเยื่อ ในการตรวจหาฟันผุด้านประชิดของฟันกรามน้ำนม
ผู้วิจัยหลัก	: นางสาวปิยนุช คำมูล
สังกัดหน่วยงาน	: คณะทันตแพทยศาสตร์
ผู้ร่วมวิจัย	: ผศ.ทพญ.ดร.ศิริลาวิทย์ โต๊ะนาค ทพญ.ดร.จุฑามาศ ดีโพธิ์ ทพญ.สุปิยญา นัยวิกุล
วิธีทบทวน	: แบบเร่งรัด
รายงานความก้าวหน้า	: ส่งรายงานความก้าวหน้าอย่างน้อย 1 ครั้ง/ปี หรือส่งรายงานฉบับสมบูรณ์หากดำเนินการเสร็จสิ้นก่อน 1 ปี
เอกสารรับรอง	<ol style="list-style-type: none"> IF 01 (Human Material Study) เวอร์ชัน 3.0 วันที่ 20 กรกฎาคม 2565 IF 02 Conflict of interest and Funding Form เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565 IF 03 (สำหรับผู้ปกครอง) เวอร์ชัน 3.0 วันที่ 20 กรกฎาคม 2565 IF 05 ประวัติผู้วิจัย เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565 IF 06 Budget เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565 โครงการวิจัยฉบับเต็ม เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565 แบบบันทึกข้อมูล เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565 แบบบันทึกข้อมูลการอ่านภาพรังสี เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565 แบบบันทึกข้อมูลการอ่านภาพพยาธิวิทยา เวอร์ชัน 2.0 วันที่ 01 กรกฎาคม 2565
	<p>ลงนาม:  (นายแพทย์สมบูรณ์ ตันสุกสวัสดิ์กุล) ประธานคณะกรรมการจริยธรรมการวิจัยในมนุษย์ มหาวิทยาลัยนเรศวร</p>
วันที่รับรอง	: 21 กรกฎาคม 2565
วันหมดอายุ	: 21 กรกฎาคม 2566
<p>ทั้งนี้ การรับรองนี้มีเงื่อนไขดังที่ระบุไว้ด้านหลังทุกข้อ (ดูด้านหลังของเอกสารรับรองโครงการวิจัย)</p>	

Tooth ID number	Group no. (1-7)	Tooth sequence (1-8)	surface	Radiographic score (0-5): <u>EOBW</u>				Radiographic score (0-5): <u>IOBW</u>			
				Observer 1		Observer 2		Observer 1		Observer 2	
				1st reading	2nd reading	1st reading	2nd reading	1st reading	2nd reading	1st reading	2nd reading
7	5	2	M	3	3	4	4	0	0	3	3
			D	5	5	5	5	4	4	4	4
8	5	4	M	3	3	4	3	3	3	2	2
			D	0	3	4	4	0	0	0	0
9	7	6	M	4	4	4	4	4	4	4	4
			D	5	5	5	5	0	0	0	0
10	1	6	M	0	0	0	0	0	0	0	0
			D	4	4	4	4	4	4	4	4
11	6	1	M	5	5	5	5	4	4	4	4
			D	0	0	0	0	0	0	0	0
12	5	7	M	3	4	2	2	4	4	4	4
			D	5	5	5	5	5	5	5	5
13	7	3	M	0	3	0	0	3	3	3	3

Tooth ID number	Group no. (1-7)	Tooth sequence (1-8)	surface	Radiographic score (0-5): <u>EOBW</u>				Radiographic score (0-5): <u>IOBW</u>					
				Observer 1		Observer 2		Observer 1		Observer 2			
				1st reading	2nd reading	1st reading	2nd reading	1st reading	2nd reading	1st reading	2nd reading		
14	7	1	D	5	5	5	5	5	5	5	5	5	
			M	5	5	5	5	2	2	2	2	3	3
15	1	4	D	0	0	0	0	0	0	0	0	0	0
			M	4	4	4	4	4	4	4	4	4	4
16	5	5	D	0	0	0	0	0	0	0	0	0	0
			M	4	4	4	4	4	4	4	4	4	4
17	7	5	D	2	2	2	2	1	1	1	1	1	1
			M	5	5	5	5	0	0	0	0	0	0
18	4	8	D	0	0	0	0	0	0	0	0	0	0
			M	0	3	0	0	0	0	0	0	0	0
19	3	7	D	3	3	3	3	3	3	3	3	3	3
			M	0	0	0	0	0	0	0	0	0	0
			D	3	3	4	4	4	4	4	4	4	

Tooth ID number	Group no. (1-7)	Tooth sequence (1-8)	surface	Radiographic score (0-5): <u>EOBW</u>				Radiographic score (0-5): <u>IOBW</u>					
				Observer 1		Observer 2		Observer 1		Observer 2			
				1st reading	2nd reading	1st reading	2nd reading	1st reading	2nd reading	1st reading	2nd reading		
53	6	2	D	0	0	3	3	0	0	0	0	1	0
			M	0	0	0	0	0	0	0	0	0	0
54	6	4	D	5	5	5	5	4	4	4	4	4	4
			M	5	5	5	5	4	4	4	4	4	4
55	6	8	D	2	2	2	2	1	1	1	1	1	1
			M	5	5	5	5	0	0	0	0	0	0
56	6	7	D	4	4	4	4	4	4	4	4	4	4
			M	3	4	0	0	3	3	3	3	3	3
			D	5	5	5	5	4	4	4	4	4	4

Data of histopathological examination

Tooth ID number	Surface	Histological score (0-4)		Cavitation 0=sound, 1=non-cavitated, 2=cavitated
		1st reading	2nd reading	
1	M	3	3	2
	D	2	2	2
2	M	3	3	2
	D	4	4	2
3	M	3	4	2
	D	3	3	2
4	M	3	3	2
	D	3	3	2
5	M	1	2	1
	D	3	3	2
6	M	4	4	2
	D	2	2	1
7	M	3	3	2
	D	4	4	2
8	M	3	3	2
	D	3	3	2
9	M	4	4	2
	D	0	0	0
10	M	0	0	0
	D	4	4	2
11	M	4	4	2

Tooth ID number	Surface	Histological score (0-4)		Cavitation
		1st reading	2nd reading	0=sound, 1=non-cavitated, 2=cavitated
	D	2	2	1
12	M	4	4	2
	D	4	4	2
13	M	3	3	1
	D	0	0	0
14	M	3	3	2
	D	2	2	1
15	M	4	4	2
	D	1	2	2
16	M	4	4	2
	D	2	2	1
17	M	2	2	1
	D	2	2	1
18	M	0	0	0
	D	3	3	2
19	M	0	0	0
	D	4	4	2
20	M	3	3	2
	D	2	2	1
21	M	4	4	2
	D	0	0	0
22	M	4	4	2
	D	1	1	1

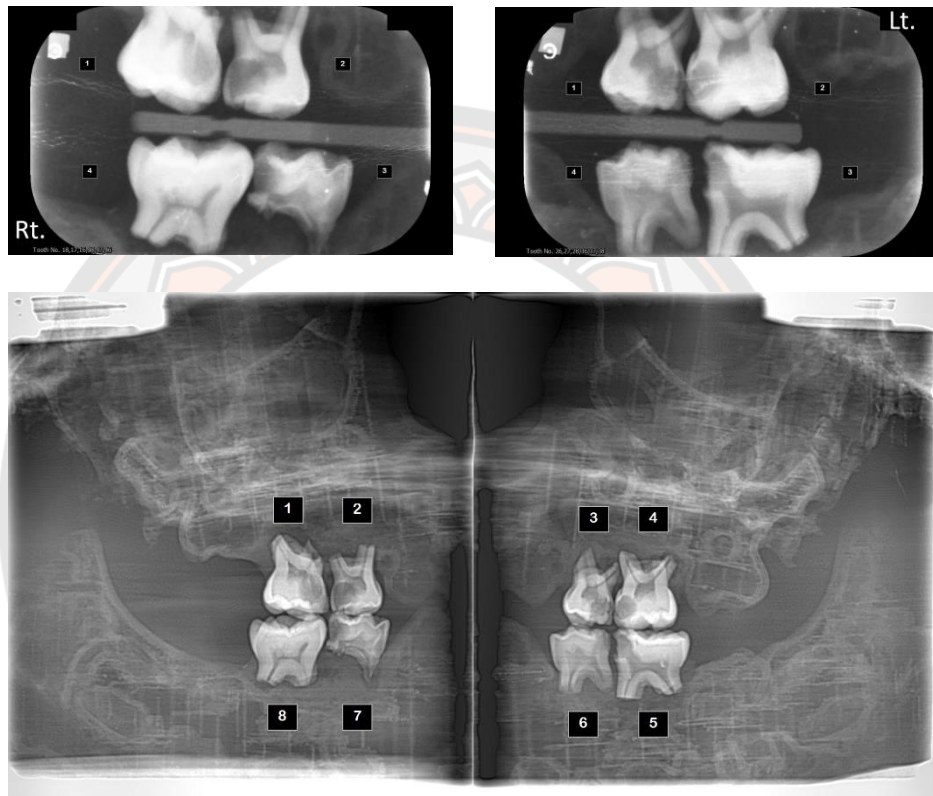
Tooth ID number	Surface	Histological score (0-4)		Cavitation 0=sound, 1=non-cavitated, 2=cavitated
		1st reading	2nd reading	
23	M	0	0	0
	D	0	0	0
24	M	4	4	2
	D	2	2	2
25	M	4	4	2
	D	2	2	2
26	M	1	1	1
	D	0	0	0
27	M	0	0	0
	D	4	4	2
28	M	0	0	0
	D	4	4	2
29	M	3	3	2
	D	4	4	2
30	M	2	2	2
	D	4	4	2
31	M	4	4	2
	D	1	1	1
32	M	1	1	1
	D	4	4	2
33	M	2	2	1
	D	4	4	2
34	M	0	0	0

Tooth ID number	Surface	Histological score (0-4)		Cavitation
		1st reading	2nd reading	0=sound, 1=non-cavitated, 2=cavitated
	D	4	4	2
35	M	2	2	1
	D	4	4	2
36	M	0	0	0
	D	4	4	2
37	M	0	0	0
	D	4	4	2
38	M	4	4	2
	D	1	0	1
39	M	0	0	0
	D	4	4	2
40	M	0	0	0
	D	4	4	2
41	M	3	3	2
	D	4	4	2
42	M	4	4	2
	D	3	3	2
43	M	4	4	2
	D	2	2	1
44	M	2	2	1
	D	4	4	2
45	M	4	4	2
	D	0	0	0

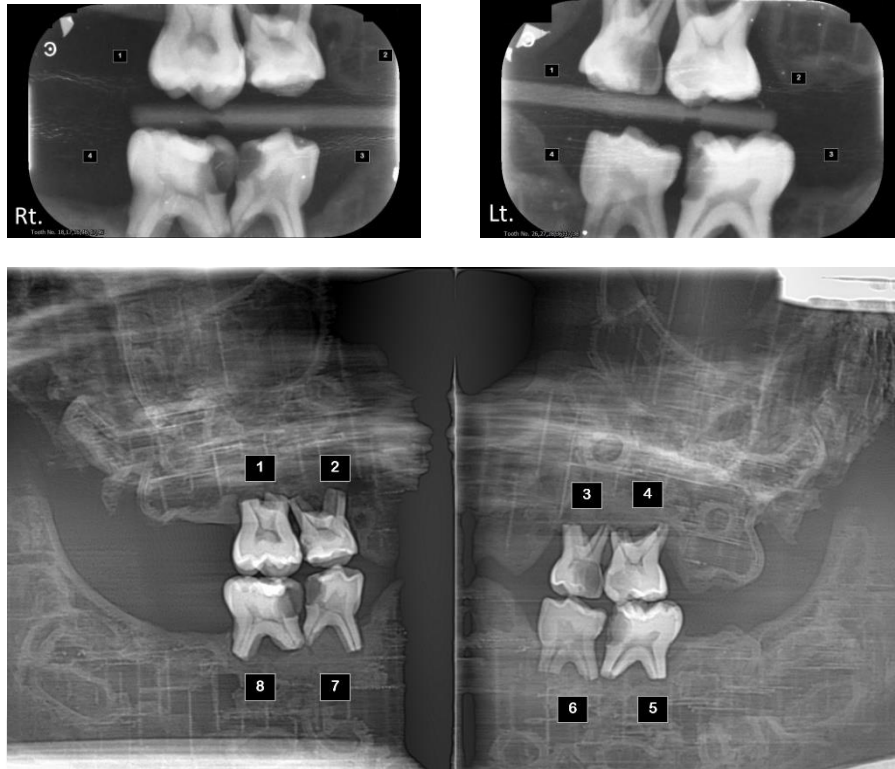
Tooth ID number	Surface	Histological score (0-4)		Cavitation
		1st reading	2nd reading	0=sound, 1=non-cavitated, 2=cavitated
46	M	0	0	0
	D	4	4	2
47	M	2	2	1
	D	3	3	2
48	M	2	2	1
	D	4	4	2
49	M	4	4	2
	D	0	0	0
50	M	3	3	1
	D	4	4	2
51	M	0	0	0
	D	4	4	2
52	M	4	4	2
	D	3	3	1
53	M	0	0	0
	D	4	4	2
54	M	4	4	2
	D	3	3	1
55	M	1	1	1
	D	4	4	2
56	M	3	3	2
	D	4	4	2

Radiographic images

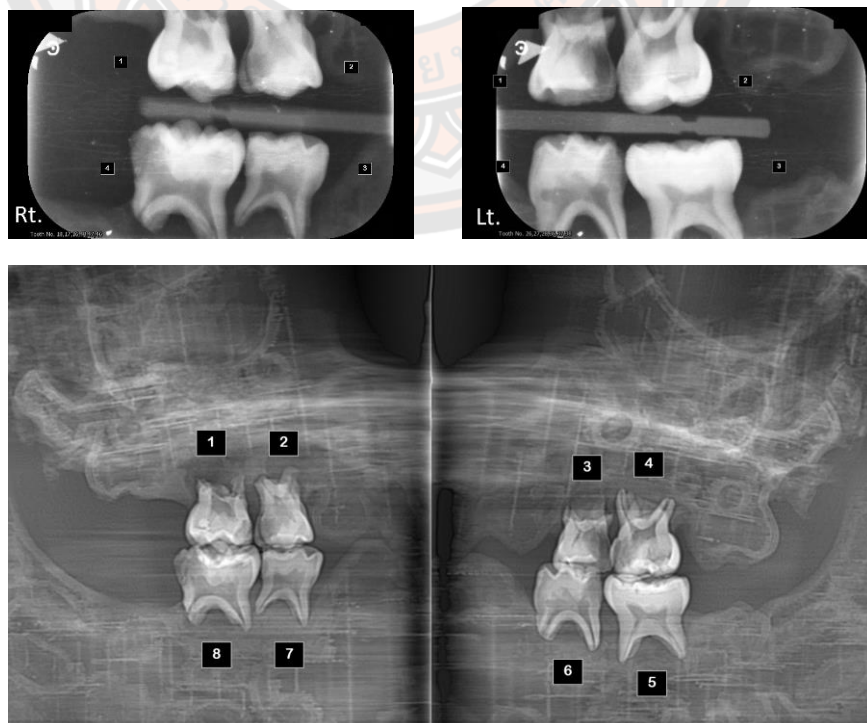
Group 1



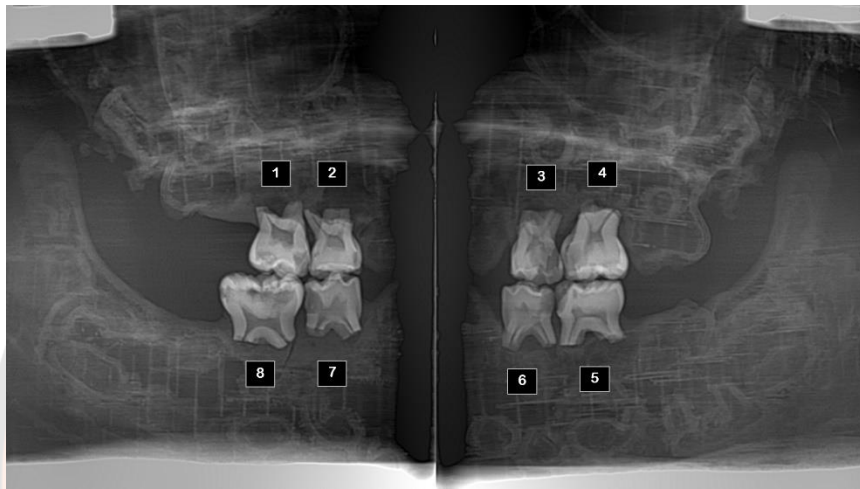
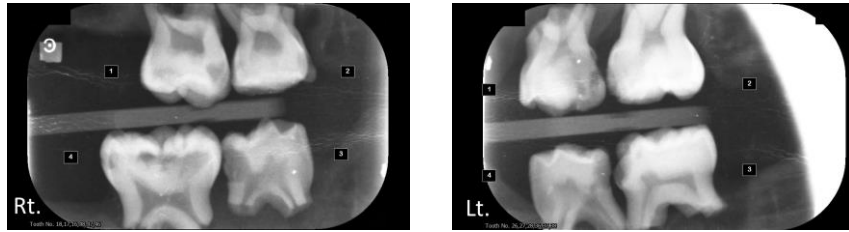
Group 2



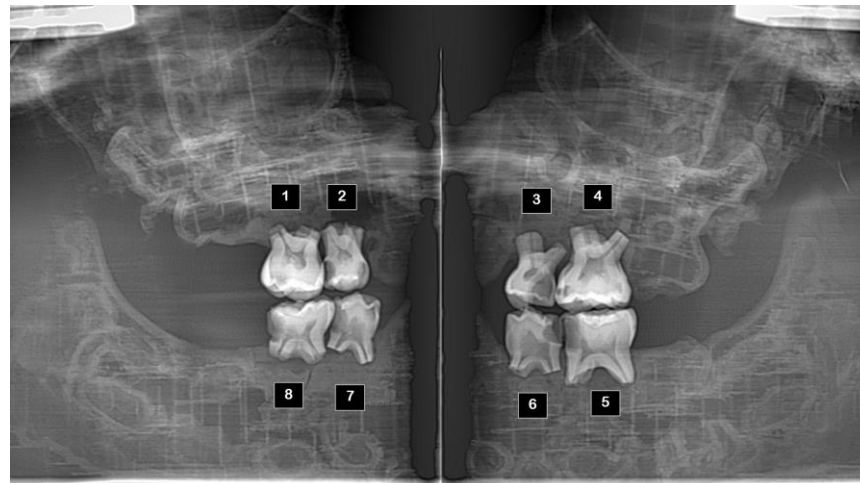
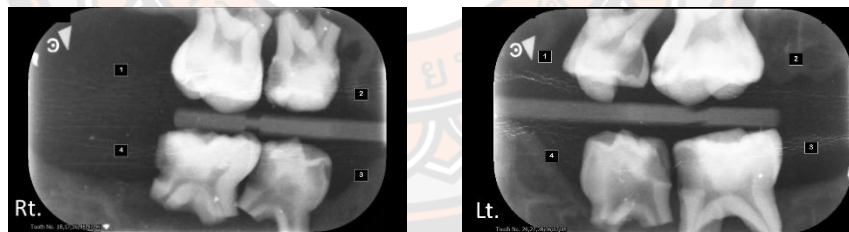
Group 3



Group 4



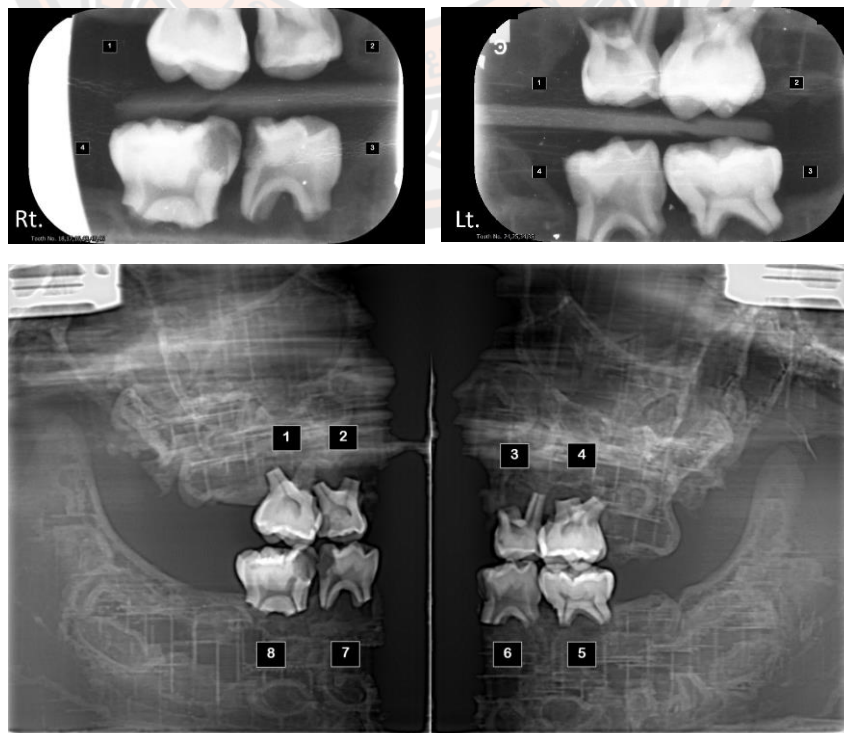
Group 5



Group 6



Group 7



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