Relationship of the macroscopic, histological, and radiographic appearance of interproximal lesions in human teeth: in vitro study using artificial caries technique

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Introduction

It is well accepted that the use of bitewing radiography is an important adjunct in the diagnosis of interproximal caries. However, the relationships between the macroscopic, clinical, and radiographic appearance of a carious lesion and its true extent in the tissues may not be fully realized by the clinician, especially since there is both confusion and controversy in the literature.

In a detailed in vitro investigation on 580 extracted teeth, Marthaler and Germann found that when radiolucencies were limited to the outer enamel, frank cavities were present in 34 percent of the teeth. When the bitewing radiolucencies extended into the inner aspects of the enamel, cavities were present in 66 percent of the teeth. This demonstrates just how advanced lesions really are in spite of what can appear to be "early" detection by radiography. These workers also showed that when a radiolucency was visible in the outer half of the dentin, small cavities were present in 87 percent of the surfaces. All of the radiographs in the above study were taken without using a soft tissue simulator and therefore represented a greater degree of sensitivity than could be achieved clinically.

It was also reported by Leijon that a greater number of carious lesions could be detected by extraoral inspection with the unaided eye compared with dental radiographs taken extraorally, even without using a soft tissue simulator. When radiographs were taken clinically, an additional number of radiolucencies were masked by soft tissues. Of 169 approximal surfaces diagnosed as sound enamel by in vitro radiography, macroscopic inspection revealed 50 white spot lesions. When these teeth were radiographed again, taking seven different exposures by rotating each tooth around its axis, 27 of the 50 lesions were made visible radiographically. This procedure could not, of course, be carried out under clinical conditions. Even attempting to change the radiographic angle slightly in vivo would result in overlap of approximal surfaces.

Backer Dirks has shown that proximal enamel lesions may remain limited to the enamel on radiographs for four years or more. If a correspondingly slow development of small lesions not yet observable on radiographs is assumed, a large number of initial lesions may accumulate within a few years without becoming perceptible on radiographs.

Darling obtained a series of teeth having lesions of varying sizes and radiographed them in vitro. He concluded that bitewing radiographs were unlikely to show the lesion before the dentin was involved. Gwinnett showed that caries frequently involved more than half the depth of the enamel before any radiographic change was detected on a bitewing radiograph. This was found to be the case irrespective of KVP value, exposure time, or processing procedure. In many cases, lesions involved the full thickness of the enamel and extended into the dentin while only a small area of radiolucency was seen on the radiograph. This study, therefore, emphasized the relative insensitivity of the clinical radiographic technique. In a similar study Buchholz concluded that when the radiograph demonstrated the smallest perceptable indication of a lesion, histological examination showed extensive demineralization in the dentin.

Of all radiographic methods, bitewing radiography appears to be the technique of choice for the detection of interproximal lesions. Hurlbert and Wuehrmann carried out a study comparing the detection of interproximal carious lesions using panoramic and standard radiography. They concluded that panoramic radiographs alone were ineffective diagnostic aids in the detection of small interproximal lesions. They found that the best radiographic survey, in terms of numbers of radiographic enamel lesions detected, was the combination of periapical plus bitewing radiographs. For lesions extending into the dentin radiographically, all combinations except panoramic radiographs used alone showed comparable results.

Thus, many workers have shown that under clinical conditions, small approximal lesions are more likely to be detected on bitewing radiographs than upon clinical examination using a mirror and an explorer. However, if approximal tooth surfaces are examined macroscopically on extracted teeth, more lesions will be detected with the unaided eye than on bitewing radiographs. Thus, it appears that for the in vivo or clinical situation where teeth are in approximal con-
A molar and premolar tooth painted with an acid resistant varnish and set up in interproximal contact in a silicone block at commencement of the study. Window regions of enamel have been left exposed on the mesial and distal proximal surfaces for the creation of artificial caries-like lesions.

In contrast, a bitewing radiograph is the most sensitive method of diagnosing interstitial carious lesions. If, on the other hand, the approximal surface of a tooth can be viewed directly due to loss of its neighbor, then this is a more sensitive method of diagnosing the presence of a lesion. Although these facts have been known for many years, they do not by themselves indicate at what stage a small lesion must be at before it can be diagnosed on a radiograph, or how extensive a lesion must be before it produces the characteristic “white spot” appearance macroscopically. The aim of this in vitro study was to attempt to correlate factors such as lesion size, macroscopic, and radiographic appearance. Since baselines using sound enamel surfaces were required prior to investigating lesion initiation and progression, an artificial caries technique was employed. This acidified gel technique has been described previously by Silverstone and is the only one capable of creating lesions in human enamel which appear indistinguishable from natural lesions when examined histologically and by ultra-structural techniques. The results presented in this paper are part of a larger series of experiments.

Methods and Materials

Human molar and premolar teeth which appeared caries-free upon macroscopic examination were selected for these studies. After cleaning the teeth with pumice powder and a soft brush using a slow-speed handpiece with a conventional dental engine, proximal surfaces were examined with incident illumination using a stereo-zoom dissecting microscope. Only teeth having intact proximal surfaces which appeared free from caries or stain were used. Teeth were then grouped together into pairs in such a manner that a good interproximal contact resulted. Each pair of teeth was then set up into a silicone block such that the tooth crowns were in contact while the roots were retained within the silicone block. Thus, a simple replica of the clinical situation was achieved with each pair of teeth (Figure 1a). Due to the elastic nature of the silicone material, either or both of the teeth from each silicone block could be removed, and returned to its original position. In this way the identical contact region was maintained for each tooth pair.

After this, the teeth were painted with an acid-protective varnish (Figure 1a) covering the roots and crown with the exception of the area of interproximal contact (Figure 1b). A corresponding window of enamel was left unpainted on the opposite noncontact proximal surface of each tooth pair. Therefore each tooth had a mesial and distal window region of enamel exposed for the production of artificial caries-like lesions.

Tooth pairs were photographed and baseline bitewing radiographs taken (Figure 2) at 90, 70 and 50 KVP, 10 ma, and with exposure times of 0.30, 0.36, 0.41 and 1.00 seconds. No soft tissue simulator was employed in the in vitro radiographic technique.

After removal from their respective silicone blocks, teeth were then exposed to an artificial caries technique consisting of acidified gelatin gels. A series of 10 percent gelatin gels were employed, acidified to pH 4.0 with lactic acid. Teeth were removed for examination after exposure periods of 4, 8, 10, 12 and 14 weeks. On removal from the artificial caries medium, teeth were washed, dried, and inserted into their respective
silicone blocks. Bitewing radiographs were then re-taken using the same series of parameters employed previously. On removing teeth from their silicone blocks, each proximal surface was photographed after removal of the varnish. In order to continue with lesion progression, teeth were carefully revarnished where necessary and replaced into a fresh aliquot of the artificial caries medium. At various exposure times, undemineralized longitudinal sections were obtained so as to examine the histological features of lesions.

In some cases a single, thin, undemineralized section was removed from the tooth for histological examination. The cut faces of the remaining tooth halves were then varnished so that only the surface of the lesion was once again exposed. Specimens were then replaced into the artificial caries medium for lesion progression. On removal of the tooth halves after this further exposure, they were inserted into the silicone blocks and photographs and bitewing radiographs taken as before. By taking another single section from the specimen, the degree of lesion progression could be ascertained histologically and compared to the radiographic findings. This technique was made possible by employing a special microtome, the Silverstone-Taylor Hard Tissue Microtome, which is able to remove single or multiple undemineralized sections at 70-80 µm thickness with no damage to the lesion (Figure 3).

Histological examination of ground sections was carried out using a polarizing microscope. A series of aqueous media and a range of alcoholic inhibition fluids was employed so as to calculate the pore volume of lesions and the presence and distribution of the various histological zones of the enamel lesion. Micro-radiographs were also taken of sections using Cu Kα radiation on Kodak High Resolution Film.

Results

Figure 4 shows the results of one series of experiments carried out on the pair of teeth shown previously at baseline in Figures 1 and 2. Figure 4a shows the teeth at the completion of the experiment after a total of 14 weeks in the artificial caries medium. The varnish has been removed from the teeth and they have been replaced into their silicone block. Figure 4b shows the bitewing radiograph of the tooth pair at completion, taken at 70 KVP with an exposure time of 0.36 seconds. These conditions produced the most sensitive results with the in vitro radiographic technique. With the exception of a small area of radiolucency on the distal surface of the molar tooth, there is no radiographic evidence of caries. This radiograph should be compared with the baseline result shown in Figure 2. Figure 4c is a diagram of the two teeth as seen on the radiograph highlighting the two proximal surfaces that are to be examined in more detail; the mesial and distal surfaces of the molar tooth. Figure

Figure 2. A bitewing radiograph of the pair of teeth shown in Figure 1a. This is a baseline radiograph taken at the commencement of the study.

Figure 3. The Silverstone-Taylor Hard Tissue Microtome. With this apparatus it is possible to remove thin undemineralized unembedded sections from the window regions. Since the sections are cut 70-80 µm in thickness with no damage to the lesion area, it is possible to examine the progression of lesions by removing sections after various exposures to the artificial caries medium.
Figure 4. Results of one series of experiments carried out on the pair of teeth shown previously at baseline in Figure 1a. 
4a. This shows the teeth at the completion of the experiment after a total of 14 weeks in the artificial caries medium. The 
varnish has been removed from the teeth and they have been replaced into their silicone blocks. 4b. This shows the bite-
wing radiograph of the tooth pair at the completion of the experiment. With the exception of a small area of radiolucency 
confined to the outer enamel on the distal surface of the molar tooth, there is no radiographic evidence of caries. This 
should be compared with the baseline radiograph shown in Figure 2. 4c. Diagram showing the two proximal surfaces 
which are to be examined in more detail; the mesial and distal surfaces of the molar tooth. 4d. The distal surface of the 
molar tooth showing the artificial “white spot” lesion. This lesion was visible as a small radiolucent area on the bitewing 
radiograph. 4e. The mesial surface of the molar tooth showing the presence of a “white spot” lesion. This lesion was not 
detected on the radiograph. 4f. Longitudinal ground section through the distal surface of the molar tooth examined with 
the polarizing microscope after imbibition of the section with water (x50). The lesion is extensive, extending the full 
thickness of the enamel and passing into the dentin. 4g. Longitudinal ground section showing the mesial surface of the 
molar tooth after imbibition with water and examined in polarized light (x50). This lesion is not as extensive as the one of 
the distal surface of the same tooth. However, the advancing front of the body of the lesion extends two-thirds through 
the enamel thickness. The advancing front of this lesion as seen after imbibition with quinoline extended a further 100 
μm. This lesion has a mineral loss in excess of 25 percent and yet there was no indication of its presence on the bitewing 
radiograph.
4d is a photograph of the distal surface of the molar tooth showing the artificial “white spot” lesion. Both this lesion, and the one produced on the mesial surface of the molar (Figure 4e), are typical of the macroscopic appearance of a “white spot” lesion and are seen in contrast to the sound enamel. While the lesion on the distal surface (Figure 4d) showed as a small radiolucent area in the outer enamel on the bite-wing radiograph, there was no radiographic indication of the presence of the lesion on the mesial surface (Figure 4e) of the same tooth. (See cover illustrations)

Histologically, the lesion on the distal surface appears extensive (Figure 4f), extending through the full thickness of the enamel and passing into the dentin. The dark (positively birefringent) region is the body of the lesion which has in excess of 25 percent mineral loss. The lesion on the mesial surface of the same tooth is also extensive histologically (Figure 4g) but to a lesser extent than the one on the distal surface. However, the advancing front of the body of the lesion as seen on the photomicrograph extends two-thirds of the distance through the depth of the enamel. The advancing front of this lesion, as seen after imbition with quinoline, extended a further 100 μm approaching the enamel-dentin junction but not reaching it. This lesion too has a mineral loss in excess of 25 percent and yet there was no radiographic evidence of the lesion on the bitewing radiograph.

Figure 5 shows a pair of premolar teeth used in the experiments. The bitewing radiograph taken at the completion of the experiment (Figure 5a) shows three proximal areas of radiolucency. The two proximal surfaces in contact each show a small radiolucency which appears to be confined to the outer half of the enamel. The diagram in Figure 5b shows that it is these two approximal lesions that are to be examined in more detail. Figure 5c shows a photograph of the respective mesial and distal surfaces of the two teeth illustrating well marked “white spot” lesions. Both lesions have a white opaque border zone with a more darkly stained internal area. Figures 5d and 5e show microradiographs taken of longitudinal ground sections from these lesions. In both cases the enamel has been

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**Figure 5a (Top).** Bitewing radiograph of a pair of premolar teeth taken after the formation of artificial caries-like lesions. Radiolucent regions can be seen on both the mesial and distal proximal surface of the larger premolar tooth whereas its neighbor shows a radiolucent lesion on the mesial surface only. **5b (Line drawing).** Diagram showing the areas of interest to be examined in more detail with this pair of teeth. These are the lesions contained within the two surfaces in contact. **5c (Teeth on fabric).** This shows the macroscopic appearance of the two “white spot” lesions after removing the varnish from the teeth. Both lesions are readily visible by naked eye. **5d (Lower left).** This is a microradiograph taken from a longitudinal ground section of the lesion on the mesial surface of the small premolar tooth. The body of the lesion is seen to have penetrated into the dentin and the enamel has been demineralized considerably. The radiographic evidence of the lesion showed it to be limited to the outer half of the enamel thickness. **5e (Lower right).** Microradiograph of the lesion on the distal surface of the large premolar tooth demonstrating the presence of an extensive lesion. This lesion too has penetrated into and demineralized the dentin. This lesion appeared to be confined to the outer half of the depth of the enamel on the bitewing radiograph.
6a. Diagram to show the correlation between the macroscopic appearance of a proximal surface of a premolar tooth and its appearance on a bitewing radiograph.

6b. Macroscopic appearance of the mesial surface of a mandibular first premolar tooth showing the appearance of an artificial "white spot" lesion. The varnish has been removed from the crown so that the lesion is seen in contrast to the sound enamel.

6c. Microradiograph of the same premolar tooth showing no evidence of radiolucency on the mesial surface containing the lesion seen in b.

6d. Microradiograph showing the mesial surface of the longitudinal ground section taken from the premolar tooth. An extensive lesion can be seen in which the body of the lesion has penetrated to a depth of 700 μm. In spite of the lesion extending through three-quarters of the enamel depth, with a considerable degree of demineralization, there is no evidence of this lesion on the bitewing radiograph. Because it has been possible to vary radiographic parameters, it is doubtful whether a clinical bitewing radiograph could accomplish this degree of "sensitivity."

demineralized extensively and both lesions extend into the dentin, showing demineralization to a depth of approximately 300 μm in the dentin. Figure 6 shows a premolar tooth from a further experiment in this series. The diagram in Figure 6a orientates the tooth surfaces as seen on macroscopic examination (Figure 6b) and by bitewing radiography (Figure 6c). Macroscopically, the "white spot" lesion can be seen very clearly and there is no difficulty identifying its periphery. However, there is no evidence of radiolucency of this mesial surface on the bitewing radiograph. The microradiograph of the same lesion taken from a longitudinal ground section (Figure 6d) shows a well-defined lesion extending approximately 700 μm into the enamel. The microradiograph shows only the advancing front of the body of the lesion, which is the region demonstrating the greatest degree of damage within the lesion. Its true advancing front is approximately 50 μm deep to this region, consisting of histological zones 1 and 2, the translucent zone and the dark zone.

Discussion

This study has shown quite clearly that bitewing radiographic examination of teeth in proximal contact is a relatively insensitive technique for the diagnosis of intact-surface carious lesions. When a lesion is first detected on a bitewing radiograph, appearing to be limited to the outer enamel, the lesion has, in reality, already penetrated several hundred micrometers into the dentin. Direct vision of the relevant cleaned and dried tooth surface by eye clearly identifies the macroscopic area as a "white spot" lesion. Since a number of parameters were varied in the radiographic technique used in this study, and since no soft tissue simulator was employed in the experiments described in this report, the radiographs must be regarded as superior with respect to sensitivity relative to those taken under standard clinical conditions. Thus, it may be concluded that the detection of a radiolucency on the proximal surface of a tooth in a bitewing radiograph implies that the lesion has already penetrated into the underlying dentin.

This study has also demonstrated that a surface
appearing caries-free on a bitewing radiograph can also have an extensive lesion present. Such lesions may have penetrated two-thirds of the depth of the enamel and have greater than 25 percent of mineral loss. Although such lesions are not detected by the radiographic technique, they are readily visible as “white spot” lesions if the cleaned and dried surface is examined by direct vision. While this is possible clinically when there is no adjacent tooth present, satisfactory macroscopic examination is not possible with normal proximal contact.

The teeth used in these experiments were from the permanent dentition. How can these results be extrapolated to teeth in the primary dentition? Recent studies by Harris and Silverstone\textsuperscript{39} comparing rates of advance of artificial lesions through primary and permanent enamel have shown a faster rate of attack in primary enamel. Progression in primary enamel was approximately 20 percent faster than in permanent enamel under identical conditions of attack. In addition, since primary enamel is only about one-half of the thickness of permanent enamel, a lesion has to travel a much shorter distance to reach the dentin. With respect to the clinical diagnosis of interproximal caries, it is more difficult to detect caries occurring between primary molars since their morphology is such that flat contact areas exist compared to contact “points” in the permanent dentition. These factors highlight the difficulties associated with early diagnosis of interproximal caries in primary molars.

Figure 7 diagrammatically shows the size of a carious lesion when viewed by different techniques. In the upper three diagrams, the lesion is seen to penetrate about two-thirds of the depth of the enamel when examined histologically. When the same longitudinal section is examined by microradiography, the lesion appears smaller since only the body of the lesion is detected by this technique. Thus, the advancing front of the lesion is comparable to examining the lesion in water and viewing the section by optical methods. The least sensitive is the use of bitewing radiography. In the upper lesion, there would be no evidence of a lesion using bitewing radiography. In the lower more extensive lesion, the bitewing radiographic appearance indicates a lesion positioned in the outer half of the enamel whereas, in fact, the lesion has penetrated into the dentin.

Figure 7. Diagram to demonstrate the size of an enamel lesion as seen by different techniques. The most sensitive is examination by optical methods, preferably polarized light microscopy, using quinoline as a mounting medium. In this manner, both the translucent zone (Zone 1) and the dark zone (Zone 2) can be seen, positioned in advance of the body of the lesion. The next sensitive is the use of microradiography which demonstrates the depth of the body of the lesion. This is comparable to examining the lesion in water and viewing the section by optical methods. The least sensitive is the use of bitewing radiography. In the upper lesion, there would be no evidence of a lesion using bitewing radiography. In the lower more extensive lesion, the bitewing radiographic appearance indicates a lesion positioned in the outer half of the enamel whereas, in fact, the lesion has penetrated into the dentin.

thin undermineralized sections has many advantages over other sectioning machines. With conventional sectioning machines a relatively thick section is removed from the tooth crown. In addition to the section being thick, the amount of tissue lost either side of the section is also large due to the thickness of the cutting disc and the vibration experienced at its periphery. Thus, it is often only possible to obtain a single section from a small white spot lesion. The true deep edge of the advancing front of the cone-shaped lesion may actually be represented on the section. More likely however, the true advancing front may be lost due to the blade passing through this region and eliminating tissue over a width of about 200 µm. Thus, a lesion appearing histologically to have penetrated two-thirds of the depth of the enamel might in reality have penetrated well into the dentin.

With the hard tissue microtome used in these studies it is possible to remove either a single section of about 80 µm in thickness or serial sections. It is possible to cut about ten serial sections from a single white spot lesion and examine them histologically without

\textsuperscript{420} \textbf{INTERPROXIMAL LESIONS: Silverstone}
the necessity for grinding the section in order to reduce its thickness. Examination of a lesion serially in this manner will show the true depth of the lesion. Thus, it is important to bear such technical considerations in mind if the true extent of a lesion is to be determined. It is suggested that this in vitro model system could be used to test the sensitivity of new radiographic systems (e.g., xeroradiography) or new developments in film type or developing techniques. This model system will allow the correlation of lesion size by the various examining procedures and will also provide a direct comparison between conventional and new radiographic techniques.

Since the lesion is always more extensive relative to its radiographic appearance, does this imply that the clinician should restore the relevant surface as soon as radiolucencies are detected? The answer is emphatically no. Dental caries is not a simple process of continuing demineralization. The production of a lesion is the result of a dynamic series of events in which phases of remineralization alternate with phases of demineralization. Many clinicians have experienced the phenomenon of radiographic reversals. This was recorded as early ago as 1938, and since then many workers have recorded reversals in diagnosis whereby small lesions detected clinically or by radiography apparently have disappeared when examined at a later date using identical criteria.

Of the four classical histological zones of enamel caries, two of them are due to remineralization phenomena as shown by Silverstone. These two zones, the surface zone (zone 4) and the dark zone (zone 2), are narrow bands occurring at the surface of the lesion and at its advancing front. When such lesions are exposed to synthetic calcifying fluids in vitro, a much greater degree of remineralization occurs and, depending on the type of calcifying fluid employed, the lesion can be remineralized throughout its entire depth. An example of such an experiment can be seen in Figures 8a and 8b. This does not imply that the lesion disappears since it is still recognizably different from sound enamel by histological and ultrastructural examination. Recent studies have shown that after remineralization of natural and artificial lesions in vitro, there is a significant increase in diameter of the individual crystals, thousands of which make up each single prism. This increase in crystal diameter, which can be 2-4 times greater than that found in the sound enamel, reduces significantly the rate of lesion progression. The presence of fluoride ions is essential in the remineralization mechanism and recent work has indicated that only low levels appear to be necessary.

This author believes that one of the main mechanisms whereby fluoride acts in caries prevention (if not the main mechanism) is in promoting remineralization. It has long been known that partially demineralized enamel takes up fluoride preferentially relative to sound enamel. Therefore, small lesions in approximal regions, not diagnosed by conventional techniques of clinical examination and radiography (as shown in this study), are able to take up significant amounts of fluoride, acting as fluoride-ion reservoirs. When conditions favoring demineralization occur, fluoride is released in addition to calcium and phosphate ions. Thus, remineralization occurs and mineral is precipitated back into the lesion. This is the reason why some lesions never progress to the stage where they are diagnosed by conventional techniques.

Silverstone has shown recently that in order for the submicroscopic crystals in enamel to increase in size relative to those of sound enamel, it is first necessary that the region is partially demineralized. Thus, remineralization can only occur after a bout of demineralization. Therefore, it might be necessary for all proximal surfaces to become carious at the histological level so that they can benefit from remineralization which, in turn, will give the region a degree of mineralization.

Figure 8a. Longitudinal ground section showing a lesion which has penetrated the full enamel thickness (x50). This section is examined in water with the polarizing microscope. The adjacent half of the lesion was exposed to a synthetic calcifying fluid in vitro (left).

Figure 8b. (Right) After exposure to the calcifying fluid the lesion shows a significant degree of mineralization. This section is examined in an identical manner to the control seen in Figure 8a. The size of the body of the lesion has been reduced dramatically. These results were accomplished by the addition of 0.06 mM fluoride ions (1 ppm) into the synthetic calcifying fluid.
of resistance towards lesion progression. Since small lesions cannot be diagnosed, their presence remains undisclosed unless they progress to the stage where they are detected by conventional means. The fact that many “caries-free” proximal surfaces may contain small lesions is highlighted by the fact that this author, in collecting small natural lesions for his research over many years, usually obtains them by sectioning teeth which appear caries-free proximally even on macroscopic examination.

The phenomenon of remineralization is emphasized in this manuscript in an effort to prevent the well-meaning clinician from attempting to restore a tooth because there is a small lesion indicated on a bitewing radiograph. A restorative approach is indicated only when there is definite radiographic evidence of lesion progression relative to a previous radiograph. Hence, the use of bitewing radiographs is an essential part of clinical diagnosis, since, in addition to the detection of interproximal lesions, they should also form the baseline from which lesion progression can be judged. Naturally it is essential that the clinician appreciates the true extent of a lesion relative to the size it may appear to be at when examined by the relatively insensitive diagnostic techniques available. However, realizing the extent of a lesion, or even the possibility that lesions exist even if they cannot be diagnosed, should in itself encourage the use of a caries-preventive approach. Thus, primary prevention at the clinical level may well be secondary prevention at the histological level.

The use of fluoride is important in enhancing remineralization although it does not appear to be necessary to use high concentrations. Recent findings support the frequent supply of low concentrations of fluoride rather than the infrequent application of very high concentrations. The old maxim of “more is better” does not apply with respect to fluoride levels in enamel and caries susceptibility, as has been thought for many years. Since it can take up to three or four years for a smooth surface lesion to progress to the stage where the dentin is invaded, there is adequate time to intercept the carious process. By employing suitable preventive methods, lesions can be successfully remineralized such that they never progress to the stage where they are diagnosed. Hence, such surfaces will remain “caries-free” at the clinical and radiographic levels of diagnosis.

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