OUTCOME ASSESSMENT OF PATIENTS WITH AMELOGENESIS IMPERFECTA WHO RECEIVED TREATMENT DURING THE MIXED DENTITION STAGE

by

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Dedication

This work is dedicated to my family.

My parents, for your support and love throughout this entire process. Thank you for always being there for me.

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Abstract

OUTCOME ASSESSMENT OF PATIENTS WITH AMELOGENESIS IMPERFECTA WHO RECEIVED TREATMENT DURING THE MIXED DENTITION STAGE

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Purpose: The purpose of this study was to assess the outcomes of dental treatment modalities of patients with amelogenesis imperfecta (AI) in the mixed dentition stage, to determine patients' oral health status post-rehabilitation, and to evaluate patients' satisfaction post-rehabilitation.

Method: A total of 74 restorations in 8 subjects with AI met the inclusion criteria. A recall appointment was scheduled for conducting evaluations on restored teeth: their clinical status (based on modified U.S. Public Health Service criteria) and periodontal evaluations (gingiva index, plaque index, and pocket depth), as well as taking clinical photographs and radiographs. At the end of the appointment, subjects were asked to answer a survey regarding their self-assessment in esthetics, function, and sensitivity. Descriptive statistics were used to summarize findings. Mixed model analysis was used to compare the periodontal status in the direct restoration and indirect restoration group, to control for multiple teeth per subject. Paired t-test was used for comparing survey responses.

Result: Among the 74 restorations placed, 67 of these restorations were present at the time of evaluation including: 31 posterior restorations (27 stainless steel crowns, 4 amalgams) and 36 anterior restorations (21 direct restorations (composite strip crowns, less than 4-surface composite resin restorations), and 15 indirect restorations (lab-fabricated resin veneers, lab-fabricated composite resin or acrylic crowns)). The remaining 7 restorations were lost. The results of the clinical evaluation of restorations showed 10 restorations were rated as unacceptable in 5 categories including: surface, form, margin, caries, and wear. The direct restoration group had a high number of unacceptable restorations (6/10). The need for retreatment was frequent in the direct restoration group (7/23). The results of the periodontal evaluation showed teeth with stainless steel crowns had a moderate score in gingival index (mean= 2.3; SD=0.69) and in plaque index (mean=2.0; SD=0.92). The indirect restoration group had a score which is within normal limits in pocket depth (mean= 2.10; SD= 0.20). Bleeding on probing was observed in every restoration group (stainless steel crown=20/23; amalgam=1/4; direct restoration=12/17; indirect restoration=14/15). PDL widening and pulp canal obliteration were common radiographic findings. However, these do not require clinical interventions rather periodic evaluations. Survey results showed a statically significant difference in subjects' satisfaction on esthetics (p= 0.002) and on sensitivity (p=0.025 while brushing, p=0.01 while eating) of their teeth post-rehabilitation.

Conclusions: During the mixed dentition stage, teeth with AI may be restored with conventional treatment modalities. Direct restorations may be successful as interim restorations and multiple repairs and replacements have to be expected before definitive restorations can be placed. Gingival inflammation and plaque accumulation were

observed following restorative treatment of patients with AI. Patients with AI were satisfied with their appearance and reported a decrease in tooth sensitivity post-rehabilitation.

Chapter I

Literature Review

Introduction

Amelogenesis imperfecta (AI) is a hereditary defect of enamel affecting both the primary and permanent dentition (Witkop, 1989). The formation of enamel is a multistep process, and enamel defects can occur at any one of those steps. By definition, AI includes only those cases where enamel defects occur in the absence of other syndromes or metabolic disorders (Witkop, 1989). It is a clinically and genetically diverse group of conditions caused by mutations in genes critical for normal enamel formation, mineralization, and maturation. The incidence of AI ranges from 1 in 718 to 1 in 14,000 depending on the population studied (Backman, 1986; Witkop, 1989). Changes in color, thickness, hardness, and smoothness have been observed in the enamel of teeth affected by AI, depending on the type and severity of the disorder.

According to Witkop, AI can be classified as hypoplastic, hypomaturation, hypocalcified, and hypomaturation-hypoplastic with taurodontism (Witkop, 1989). In hypoplastic AI, the teeth are yellowish brown in color, rough in texture, and widely spaced. In hypomaturation AI, the clinical crowns are of normal size and contact adjacent teeth, but the mottled, brown-yellow enamel is soft. In hypocalcified AI, the enamel layer may be of normal thickness, but is rough and soft and wears away quickly following tooth eruption. In hypomaturation-hypoplastic AI with taurodontism, the enamel is mottled

white-yellow-brown in color and is thin at the areas of hypomaturation. The permanent molars associated with this condition have taurodontism. In addition, other teeth may also have enlarged pulp chambers.

Although AI, by definition, affects only the enamel formation, it has multiple consequences for affected patients. Often these patients experience difficulty in maintaining oral hygiene, decreased masticatory function, and a lower self-esteem, which significantly affect their over-all quality of life (Seow, 1993; Coffield *et al.,* 2005). Furthermore, most variants of AI require extensive dental treatment, which can be time consuming and often poses a significant economic burden on their family. The clinical management of a growing child with AI at any given developmental stage may present great challenges to the patient, their parents, as well as to the oral health professionals involved. Clinicians must therefore consider treatment alternatives to balance the patient's esthetics and functional needs, the status of patient's growth and development, the financial implications for the patient's family, and the long-term prognosis.

Treatment of AI depends on the individual's specific diagnosis and phenotype. Case reports have presented different strategies including: the use of glass ionomer cements, composite resin, stainless steel crowns, lab-fabricated crowns, and even multiple extractions necessitating an overdenture (Rada *et al.*, 1990; Seow *et al.*, 1993; Rosenblum *et al.*, 1999; Yip *et al.* 2003; Akin *et al.*, 2007). Unfortunately, research on long-term follow up of restorative outcomes of patients with AI is particularly scarce. The majority of evidence relies on case reports that present treatment modalities and outcomes of only a few AI patients with or without an additional description of their family members. It is surprising to note that there is currently no standard of care established for managing

patients with AI, especially during the mixed dentition stage.

The purpose of this study was to assess the restorative treatment outcomes of various treatment modalities of patients with AI in the mixed dentition stage, to determine patients' oral health status after operative intervention, and to evaluate patients' satisfaction post-rehabilitation.

Classification of AI

The four major types of AI are hypoplastic, hypomaturation, hypocalcified, and hypomaturation-hypoplastic with taurodontism, which are based on the Witkop classification system (Witkop, 1989). However, when clinical features and inheritance pattern are taken into consideration, 15 subtypes of AI can be distinguished. These 15 subtypes are currently the most widely used and accepted AI classification system. The following are descriptions of the 15 subtypes (Witkop, 1989).

Classification of AI proposed by Witkop (1989)

Type I	**Hypoplastic**
IA	Hypoplastic, pitted autosomal dominant
IB	Hypoplastic, local autosomal dominant
IC	Hypoplastic, local autosomal recessive
ID	Hypoplastic, smooth autosomal dominant
IE	Hypoplastic, smooth X-linked dominant
IF	Hypoplastic, rough autosomal dominant
IG	Enamel agenesis, autosomal recessive
Type II	**Hypomaturation**
IIA	Hypomaturation, pigmented autosomal recessive
IIB	Hypomaturation, X-linked recessive
IIC	Snow-capped teeth, X-linked
IID	Snow-capped teeth, autosomal dominant
Type III	**Hypocalcified**
IIIA	autosomal dominant
IIIB	autosomal recessive
Type IV	**Hypomaturation-hypoplastic with taurodontism**
IVA	Hypomaturation-hypoplastic with taurodontism, autosomal dominant
IVB	Hypomaturation-hypoplastic with taurodontism, autosomal recessive

Type I Hypoplastic AI

Hypoplastic AI is characterized by a reduced thickness of enamel which may

clinically present as pitting, grooves or large enamel defects (Hu *et al.*, 2007), and is associated with less severe problems. Radiographically, normal contrast exists between enamel and dentin.

Type IA: Hypoplastic, pitted autosomal dominant

In type IA, the enamel exhibits pinpoint pits randomly observed on labial or buccal surface in the permanent dentition. Some teeth may be unaffected in both dentitions.

Type IB: Hypoplastic, local autosomal dominant

In type IB, the defects present as pits and grooves occurring in a horizontal arrangement across the middle third of the crown. Cases of type IB may affect only primary teeth or it can affect teeth in both dentitions.

Type IC: Hypoplastic, local autosomal recessive

Type IC is more severe than the dominant type. In type IC, hypocalcified enamel may occur in the hypoplastic areas. Almost all teeth are affected in both dentitions.

Type ID: Hypoplastic, smooth, autosomal dominant

In type ID, enamel is thin, hard, shiny, and smooth and varies from white to yellow-brown in color. Spacing exists between teeth, and enamel is hypocalcified at the interproximal regions. Radiographically, a thin layer of enamel can be recognized in contrast to the underlying dentin. Unerupted teeth which undergo intra-alveolar crown and/or root resorption are frequently observed. Anterior open bite occurs in about fifty percent of affected individuals.

Type IE: Hypoplastic, smooth, X-linked dominant

In affected type IE males, enamel is thin, smooth, shiny, and brown to yellow-brown in color. Radiographically, the affected male's teeth reveal a thin layer of enamel. Carrier females have alternating vertical bands of normal thick enamel, and abnormal thin enamel. Anterior open bite occurs in most males and one-third of affected females.

Type IF: Hypoplastic, rough, autosomal dominant

In type IF, enamel is thin, hard with a granular texture. The teeth lack contacts. Radiographically, a thin layer of enamel contrasts drastically with underlying dentin. Unerupted teeth with resorption of the crown may occur. Anterior open bite occurs in about fifty percent.

Type IG: Enamel agenesis, autosomal recessive

In type IG, enamel is rough, granular texture, and light yellow-brown in color. Contact between teeth is lacking. Often teeth are unerupted and partially resorbed in alveolus. Radiographically, there is no sign of enamel.

Type II Hypomaturation AI

The hypomaturation AI is characterized by normal enamel thickness but has a mottled appearance and is softer than normal enamel. Dentin is often exposed due to enamel chipping away from the crown of the tooth.

Type IIA: Hypomaturation, pigmented autosomal recessive

In type IIA, the enamel is clear to cloudy, mottled, agar-brown in color. Enamel is of normal thickness, but is softer than normal, and can be penetrated by the tip of an explorer. Radiographically, there is no contrast between

enamel and dentin. Anterior open bite occurs infrequently.

Type IIB: Hypomaturation, X-linked recessive

In affected type IE males, enamel appears chalky white in the primary teeth and mottled yellow in the permanent teeth. Enamel in affected males is soft and can be penetrated by a probe tip under pressure. Carrier females have alternating vertical bands of normal enamel, and abnormal chalky white thin enamel in the primary teeth, known as the lionization effect. Enamel of the permanent teeth in carrier females has alternating vertical bands either chalky white or opaque yellow and normal enamel.

Radiographically, the affected male's teeth show a slight decrease in contrast between enamel and dentin, while the affected female's teeth reveal no defects.

Type IIC: Snow-capped teeth, X-linked

Teeth affected by type IIC have an opaque white enamel appearance in the incisal and occlusal thirds of the crown. Both dentitions are affected. The defects exhibit an anterior to posterior distribution. That means some affected individuals show defects on maxillary incisors and canines, some other individuals have these teeth involved plus the bicuspids, and some have all the teeth involved. Mode of inherence is presumed to be X-linked, due to the majority of the results from case reports.

Type IID: Snow-capped teeth, autosomal dominant

This is possibly an autosomal dominant form, but this is based on an isolated case report of an affected kindred. Teeth affected are similar in characteristics

to type IIC.

Type III Hypocalcified AI

The hypocalcified AI is characterized by normal enamel thickness with insufficient mineralization resulting in loss of enamel after eruption. Radiographically, enamel appears less radiopaque than dentin.

Type IIIA: Hypocalcified, autosomal dominant

In type IIIA, enamel is of normal thickness, and yellow-brown in color. Shortly after eruption, the enamel becomes brown to black due to extrinsic staining. Dentin is exposed due to wear or fracture of soft enamel, but the cervical enamel may be better calcified. Therefore, the teeth are sensitive to temperature changes. Radiographically, dentin is more opaque than enamel, and crowns present with a "moth-eaten" appearance. Teeth often tend to accumulate a large amount of calculus.

Type IIIB: Hypocalcified, autosomal recessive

In type IIIB, the clinical findings are similar to those in type IIIA but with an increased severity and an autosomal recessive inheritance pattern.

Type IV Hypomaturation-Hypoplastic with Taurodontism AI

The hypomaturation-hypoplastic with taurodontism AI is characterized by hypomatured enamel in mottled yellow-brown, white appearance. Molars of affected individuals exhibit taurodontism with enlarged pulp chambers.

Type IVA: Hypomaturation-hypoplastic with taurodontism

Type IVA is distinct from the tricho-dento-osseous syndrome. The affected enamel is hypomatured with mottled yellow-brown, white appearance, and often

exhibits pitting on labial surfaces. Large pulp chambers may occur in single rooted teeth.

Type IVB: Hypoplastic-hypomaturation with taurodontism

In type IVB, the enamel is thin and predominantly hypoplastic in areas of hypomaturation. The teeth show taurodontism similar to those in type IVA.

Genetic Etiology

The different clinical manifestations of AI have specific gene mutations associated with each phenotype. Mutations in four candidate genes have been proven to cause AI: amelogenin (AMELX), enamelin (ENAM), kallikrein4 (KLK4) and enamelysin (MMP-20). Mutations in the AMELX gene encoding for the amelogenin-protein cause most of the X-linked hypoplastic AI (Kim *et al.,* 2004). Depending on the specific mutation, the phenotype associated with AMELX mutation can be smooth hypoplastic, hypocalcified, or hypomaturation (Wright *et al.,* 2003; Kim *et al.,* 2004). The ENAM mutations encoding for the enamelin protein result in an autosomal dominant or recessive hypoplastic AI with the phenotype ranging from relatively minor, localized enamel pitting to severely hypoplastic enamel (Hart *et al.,* 2003; Kim *et al.,* 2005a). Mutations have been reported in the KLK4 and MMP-20 genes which code for the kallikrein and enamelysin proteinases cause a hypomaturation AI that is transmitted as an autosomal recessive trait (Hart *et al.,* 2004; Kim *et al.,* 2005b). These gene mutations, however, account for only a quarter of all AI cases (Kim *et al.,* 2006; Lee *et al*., 2008).

The hypomaturation-hypoplastic with taurodontism AI (AIHHT) is a variation of tricho-dento-osseous syndrome (TDO). The principal clinical features of TDO include

kinky hair at birth, osteosclerosis, brittle nails, enamel hypoplasia, and taurodontism. Mutations in the distal-less homeobox 3 (DLX3) genes cause TDO (Hart *et al.,* 1997). Price *et al.* reported that AIHHT is a distinct condition and not due to a DLX3 mutation. (Price *et al.,* 1999). However, Dong *et al.* reported a case of TDO syndrome caused by a 2-bp deletion in the DLX3 that was classified as AIHHT (Dong *et al.,* 2005). This 2-bp mutation was later identified to be the causative factor of a family with TDO (Lee *et al*., 2008). It is likely that the clinical diagnosis of a family in Dong's study should have been TDO instead of AIHHT. As more family members with AIHHT and TDO are investigated, the genotype and phenotype correlation of families with DLXE3 mutations may be better demonstrated.

Recently, Lee *et al.* identified mutations in family with sequence similarity 83 member H (*FAM83H)* gene responsible for autosomal dominant hypocalcified amelogenesis imperfecta (Lee *et al.,* 2008). Unlike other genes that cause AI, *FAM83H* does not encode an enamel matrix protein. Its location inside the ameloblast and its function are completely unknown. Mutations of *FAM83H* gene account for another 25% of the AI cases, indicating that more AI candidate genes still need to be identified. Identification of mutation genes and cataloging mutations under different types of AI will provide a better understanding of enamel anomalies.

The Histologic and Biochemical Characteristics of the Enamel Affected by AI

Various methods to evaluate the teeth with AI have been developed. The teeth with AI can be assessed by scanning electron microscopy and ground sections. Gopinath *et al.* reported that the ground sections of the AI teeth revealed the histologic characteristics

such as hypoplastic enamel layer, positively birefringent, generalized pitting, roughness with an irregular, general cracked border and porous enamel surface (Gopinath *et al.,* 2004). Seymen *et al.* evaluated AI teeth by using scanning electron microscopy and observed irrregular enamel, irregular orientation of crystallites and empty zone between the crystallites in hypoplastic type of AI (Seymen *et al.,* 2002). These findings supported the theory that AI affects the enamel crystallites formation, which result in abnormal crystallite morphology.

Few studies focused on the mineral and protein composition of AI enamel to better define AI. Wright *et al.* found that hypocalcified and hypomaturation AI can have substantial decreases in the enamel mineral content while hypoplastic AI enamel varied from normal to reduced mineral content compared with normal enamel (Wright *et al.,* 1995). This decreased mineral content was associated with the increased protein content in AI enamel (Wright *et al.,* 1995). These findings may help categorize AI and provide insights on the specific mechanisms that lead to abnormal enamel formation.

This altered enamel structure may influence the ability of teeth with AI to adequately bond to adhesive dental materials. It has been speculated that the increased protein content interfere with the development of a typical etching pattern using 37% phosphoric acid (Venezie *et al.,* 1994). This area of restorative dentistry for AI has not been well investigated. Seow and Amaratunge (1998) performed acid etching on the extracted teeth affected with pitted hypoplastic, smooth hypoplastic, X-linked, and hypocalcified AI. They concluded that the lack of typical etching patterns in the hypoplastic AI may be the result of an abnormal prism structure, or the standard acid etching time and/or concentration may be inappropriate for the abnormal enamel (Seow and Amaratunge,

1998). However, it is interesting to note that their results also showed the presence of the typical etch patterns in most variants of AI, suggesting that bonding of composite resin may be feasible in most patients with AI (Seow and Amaratunge, 1998). The high failure rate of composite resin bonding on AI teeth could be due to factors other than bonding failure, such as cohesive failure occurring at enamel, DEJ, or dentin level.

Clinical Implication of AI

Although AI primarily affects enamel formation, a variety of clinical implications may also be present, such as low caries susceptibility, rapid attrition, excessive calculus deposition, and gingival hyperplasia (Sundell, 1986; Wright, 1992; Poulsen *et al*, 2008).

The severity of clinical problems varies with each type of AI. Low caries susceptibility has been reported in children with severe hypoplastic and hypomineralized AI (Sundell, 1986b). While Sundell stated that the bacteriological and salivary data in the AI patients were inadequate to explain low caries susceptibility (Sundell, 1986b), it was suggested that additional investigations which focus on determining the difference of oral microflora between affected and unaffected individuals would be informative. Sundell also speculated that atypical crown morphology with less dramatic fissures, loss of proximal contacts, and rapid attrition commonly associated with hypoplastic AI teeth may contribute toward low caries susceptibility (Sundell, 1986b).

Rapid and excessive calculus formation has been reported as a common finding related to the hypomaturation and hypocalcified types of AI (Wright, 1992). In a review, Wright speculated that the factors contributing to excessive calculus accumulation may include: a rough enamel surface, altered salivary flow rate, composition, oral hygiene

abilities occurring secondary to dental sensitivity, and altered oral microflora (Wright, 1992). However, there was no evidence provided to support his theory. Sundell did observe that the saliva secretion rate, pH and buffer capacity from AI individuals corresponded to children without AI (Sundell, 1986b). Moreover, the gingival condition and oral hygiene among patients with AI were reported to be poor (Sundell, 1986; Seow, 1993). It can be assumed that atypical tooth morphology and poor oral hygiene may accelerate plaque accumulation or increase tooth sensitivity, posing challenges for dental care providers.

Patients with AI are also affected by their poor esthetics, tooth sensitivity, and decrease of occlusal vertical dimensions through loss of tooth structure (Seow, 1993). AI patients may experience compromised chewing function due to tooth sensitivity and the short clinical crowns caused by attrition and/or incomplete eruption. Unfortunately, restorative treatment for patients with AI is not often provided at an early age due to issues relating to tooth sensitivity, difficulty in managing extensive treatment needs, and even cost. There is a tendency to adopt a "wait-and-see" policy, often resulting in the development of deep bite and deleterious tooth wear. The resultant deep bite, short clinical crowns and altered mesiodistal dimensions of teeth complicate treatment considerably.

Growth and Development

AI is a diverse group of genetic disorder primarily affecting the quality and/ or quantity of enamel. Non-enamel-related manifestations may also occur, including an open bite malocclusion, accelerated dental development, high prevalence of dental

impaction, congenital missing teeth, crown and/or root resorption, pulp calcification, and associated abnormalities (Seow, 1993; Seow, 1995; Collins *et al.*, 1999; Ravassipour *et al.*, 2005; Poulsen *et al.*, 2008).

Open bite malocclusion has been reported to be associated with AI. Ravassipour *et al.* stated that, among 54 AI patients, 42% of AI affected individuals and 12% of unaffected family members had dental or skeletal open bite malocclusion when compared to a general Caucasian population (5%). The severity of enamel phenotype did not necessarily correspond to the presence or severity of the open bite malocclusion. They stated that the etiology of open bite malocclusion in the different types of AI is heterogeneous. It includes factors such as abnormal eruption of posterior teeth, modifying genes affecting both the dental and craniofacial developmental processes and environmental factors (Ravassipour *et al.,* 2005).

Children with AI may also exhibit accelerated tooth eruption when compared to the unaffected population. Seow found that all subjects with AI regardless of variants showed a significant acceleration of dental age of approximately 1.13 ± 0.78 years compared with children in the control group (Seow, 1995).

Oral pathologic findings have also been reported to be associated with AI. Seow found that patients with AI had a (26.1% vs. 4.3%) higher tendency than the unaffected group to have impacted permanent teeth and associated anomalies, such as follicular cysts (Seow, 1995). The observed impacted teeth among hypocalcified and hypomaturation AI types primarily involved canines (Collins *et al.*, 1999).

Collins stated that the frequency of dental anomalies also varied in different types of AI. Hypoplastic AI frequently exhibited delayed eruption, crown resorption, and pulp

calcification. The prevalence of taurodontism was similar in individuals with AI and individuals without AI (Collins *et al.*, 1999). Taurodontism may occur as an isolated trait or as a component of a specific syndrome such as TDO syndrome (Jorgenson, 1982), Klinefelter syndrome (Jorgenson, 1982), and AI. In Collins and colleagues' study, the result did not reveal an increased prevalence of taurodontism. Therefore, they speculated that there may be specific AI types that have taurodontism but were not included in the population studied. Whether these concurrent anomalies developed as a direct consequence of the molecular defect responsible for the enamel malformation or as a result of unknown secondary factors remains to be determined (Collins, 1999). The presence of these abnormalities has apparent implications on the clinical management of these patients. Early screening for these abnormalities should be done so that interceptive treatment can be rendered to prevent further damages to the developing affected dentition.

Specific Treatment Considerations

Individuals with AI often experience concern over poor dental esthetics, tooth sensitivity, and extensive tooth attrition. Because of this, it is necessary to provide appropriate dental treatments throughout the developmental stage. During any given phase of treatment, strict oral hygiene instruction and preventive treatments are equally essential in order to prevent caries, gingivitis, and calculus formation which may exacerbate existing problems. The successful management of AI requires the cooperation and motivation of both the patient and parents because the dental treatments can extend over many years and long-term success depends on regular attendance for

dental procedures and the maintenance of optimal of oral health care.

The management of individuals affected by AI has been described as three stages in the literature (Bouvier *et al.,* 1996).

- Temporary phase — undertaken during the primary and mixed dentition
- Transitional phase – when all permanent teeth have erupted and continue till adulthood
- Permanent phase – occurs in adulthood.

In the primary dentition, the dental treatment of affected children aims to ensure favorable conditions for the eruption of the permanent teeth as well as for the normal growth of the facial bones and the temporomandibular joints (Ranta *et al.,* 1993). Upon eruption of the primary molars, stainless steel crowns are placed to prevent the development of caries and the attrition of defective enamel, while maintaining adequate space and vertical dimension of occlusion. In the primary anterior teeth, polycarbonate crowns, resin modified glass ionomers (RMGI), prefabricated crowns (stainless steel crowns with or without esthetic facing) or direct composite resin can be used as alternative restorations. When a more conservative approach is desired, RMGI is recommended in occlusal non-stress bearing areas because of its fluoride releasing and chemically retentive ability, while composites resin provide acceptable resistance to occlusal wear in stress bearing tooth surfaces (Ranta *et al.,* 1993).

In the mixed dentition, the treatment goals are to preserve tooth structures, maintain tooth vitality, decrease tooth sensitivity, establish correct interproximal and occlusal function, and improve esthetics. However, rehabilitation in the mixed dentition is complex, since teeth have different eruption sequence, and definitive treatment cannot be

rendered until complete eruption of the permanent dentition. During this stage, there is often a need to reestablish the vertical dimension of occlusion. Stainless steel crowns on the permanent first molars are often recommended because they provide sufficient and stable vertical dimension of occlusion. Casting onlays bonded onto the posterior teeth and composite resin restorations on occlusal surface have also been used as conservative approaches to increase vertical dimension of occlusion (Bedi, 1989; Harley and Ibbeston, 1993). Several treatment modalities have been reported to improve dental esthetics (Ng and Messer, 2009). Direct or indirect composite resin veneers may be used to mask the discoloration and improve the crown morphology and contact with adjacent teeth. Also, full-coverage adhesive composite resin or polycarbonate crowns have also been advocated (Kwok-Tung *et al.*, 2006; Sapir and Shapira, 2007).

In the permanent dentition, the final treatment objectives are to diminish tooth sensitivity and to restore vertical dimension of occlusion, function, as well as esthetics. The final treatment often starts as soon as clinical height of the crown and the gingival tissue have been stabilized and the pulp tissues have receded. Full mouth rehabilitation combined with a multidisciplinary approach may be advantageous (Akin *et al.*, 2007).

Prosthodontics, periodontics, orthodontics, and endodontics may be necessary. Treatment could also include orthognathic surgery (AAPD 2010). Crown lengthening and gingival recontouring may be indicated in case of short clinical crowns and gingival hyperplasia. Orthodontic treatments may be used to close interdental spaces prior to restoration and correct the anterior open bite malocclusion. Bouvier *et al*. reported an AI case that underwent orthodontic treatment successfully without any problems arising from the placing of brackets on the performed stainless steel crown and polycarboxylate crowns

(Bouvier *et al*., 1996). Root canal therapy is indicated when pulp exposures are caused by severe attrition or tooth reduction. Orthognathic surgery may be indicated in case of severe malocclusion. Consultation with the appropriate specialists may help in developing a comprehensive treatment plan for each individual.

Treatment Modalities for AI

Historically, patients with AI were treated with multiple extractions followed by dentures (Seymen, 2002). This was because of the lack of suitable restorative materials to maintain hypoplastic teeth which often had pulpal involvement soon after eruption.

The treatment approach should consider the specific AI type and underlying defect. In the patients with hypoplastic AI, enamel is usually sufficient for bonding so composite resin restoration may be successful masking discoloration and improving crown morphology (Seow and Amaratunge, 1998). In patients with hypocalcified AI, there is insufficient enamel for bonding. Glass ionomer cements and composite resin restorations might initially be successful in these cases, but the long term-prognosis is guarded as the hypocalcified enamel may fracture, causing defective margins and broken restorations. Full coverage restorations are commonly recommended for hypocalcified AI.

Numerous treatment modalities have been studied for the rehabilitation of AI patients. With the advance in techniques and increase in availability of various dental materials, many studies have shown the use of glass ionomer cements, composite resin veneers, porcelain veneers, stainless steel crowns, lab-fabricated crowns, and/or over dentures can restore the affected teeth (Renner *et al.,* 1983; Rada *et al.*, 1990; Seow *et al.*, 1993; Rosenblum *et al.*, 1999; Yip *et al.*, 2003; Akin *et al.*, 2007). It is now possible to save the

affected dentition and improve both function and esthetics in teeth affected by AI.

Intraconoral Restoration

Direct restorative materials, such as amalgam, glass ionomer cements, composite resins, resin-modified glass ionomer cements, have been advocated restoring teeth with AI. Amalgam can be used to restore small lesions in posterior teeth especially with mildly affected hypoplastic AI. However, amalgam restorations are usually unsuccessful in severely affected teeth with AI due to the fractures in defective enamel margins. Seow found that adhesive materials such as glass ionomer cements and composite resins are better retained in small restorations compared to amalgam restorations (Seow, 1993). Moretti *et al.* reported that teeth restored with resin modified glass ionomer cements markedly decreased the patient's dental sensitivity and improved chewing function and esthetics (Moretti *et al.,* 2007). Unfortunately, very little evidence exists to support the long-term use of glass ionomer cements and resin modified glass ionomer cements.

Composite veneers and composite resin restorations have been advocated to mask discoloration and improve dental esthetics. Composite resin restorations can be placed with minimal tooth preparation or no tooth preparation to preserve tooth structure and is a favorable treatment option for partially erupted teeth. Rada reported composite resins provided satisfactory esthetics and durability (Rada, 1990). Composite resin restorations were clinically successful in children with hypocalcified AI during the 36 months follow up (Sonmez *et al.*, 2009). However, a high failure rate associated with insufficient bonding between the composite resin restoration and enamel among variants of AI has been reported in the past (Seow *et al.,* 1998). Several approaches have been documented

to improve bonding strength between composite resin restoration and enamel. Venezie *et al.* found that pretreatment of enamel surfaces affected by AI with five percent sodium hypochlorite resulted in an improvement of bonding strength in vitro (Venezie *et al.,* 1994). On the other hand, Sonmez *et al.* further investigated this in the clinical setting and found that pre-treatment with sodium hypochlorite had no significant effect on the success of the adhesive restoration in the intraoral condition. In addition, Rada also recommended the use of glass ionomer cements combined with dentinal adhesives as the first layer, and restoration with a hybrid composite resin on the top (Rada, 1990). Due to this lack of consensus in the literature, there is still a need to evaluate the effectiveness of intraconoral restorations of teeth with AI.

Extracoronal Restoration

Although bonding onto the hypoplastic enamel is feasible, sufficient enamel must be available for bonding. In certain types of AI such as hypocalcified type, enamel fracture frequently results in defective restoration margins. Therefore, full coverage restorations may be a more effective method to provide maximal protection, esthetics, and function.

Stainless steel crowns are reported to be the most effective and efficient restoration in managing tooth sensitivity and restoring severely broken down primary molars and permanent molars in children (Seow, 1993; Rosenblum *et al.,* 1999). Stainless steel crowns can be placed with minimum preparation, preserving tooth structure as much as possible in preparation for a more definitive treatment in the future. Furthermore, stainless steel crowns are delivered in the same appointment, decreasing the chances of loss, fracture or shifting of teeth. However, stainless steel crowns do not have perfectly

adapted margins and as such their long-term use on the permanent teeth must be carefully considered. In order to obtain custom-made margins, casting crowns are a viable alternative for posterior teeth (Bedi, 1989). In a study comparing stainless steel crowns and casting crowns in restoring the permanent first molars affected by AI or teeth with severe enamel defects, no significant differences in quality or longevity of the restorations were found after up to 24 months of follow-up (Zagdwon *et al.,* 2003). The long-term effect of using stainless steel crowns on the permanent first molars is unknown and needs further investigation.

Casting onlays have also been suggested to protect the remaining tooth structure on the posterior teeth, and may be fabricated without tooth preparation (Bedi, 1989; Harley and Ibbeston, 1993). These restorations can be used before the teeth are fully erupted. It may be a concern that the placement of supraoccluding restorations will result in increase of the vertical dimension of occlusion and change occlusion negatively. In a study of 12 children, age 7-to 18-years old, affected by either amelogenesis imperfecta or dentinogenesis imperfecta, patients were able to re-establish their occlusion within 3 months after restoration cementation (Harley K *et al.,* 1993). To date, the long-term evaluation of the efficacy of such restoration is necessary.

Acrylic resin crowns or poly carbonate crowns were used to restore the anterior teeth. The acrylic resin or polycarbonate crowns are esthetically acceptable and less expensive. Even when there is no sufficient enamel available for bonding, acrylic crowns or polycarbonate crowns are likely to be helpful for anterior teeth, particularly in the mixed dentition (Sapir and Shapira, 2007). When the enamel defects involve proximal surfaces or decreased bonding is expected, these crowns offer reasonable esthetics and retention

due to their full coverage and the use of cement. The advantages include minimal tooth preparation and crown relining as necessary. However, their use in AI teeth has not been systemically evaluated.

For AI patient with a deep overbite, composite resin bonded restorations and veneers are not recommended as a treatment option because incisal loading creates negative impact that leads to restoration failure. Little information in the literature reports the use of stainless crown in the anterior teeth in children with deep overbite. Rosenblum reported a case using stainless steel crowns, which have been pre-fitted and then professionally veneered in a patient with 100% overbite. Rosenblum stated that this technique increased the longevity of the veneer and produced a better fitting crown (Rosenblum *et al.,* 1999).

Porcelain fused to metal (PFM) crowns for the anterior and posterior teeth are the restoration of choice for AI patients and have been reported to be successful but only in affected adults (Yip *et al.,* 2003). Ceramic crowns are also considered for anterior restorations because of its esthetics (Akin, 2007). However, those types of crowns require significant tooth reduction. Thus, the use of PFM and ceramic crowns in young permanent teeth is not recommended due to the presence of large pulp and short clinical crowns. Obtaining radiographs prior to restorative treatment is essential to determine when these restorations can be placed.

Overdenture

An overdenture is supported both by soft tissues and the roots of teeth or modified teeth. Renner *et al.* reported a case which was successfully treated by maxillary

overdenture (Renner *et al.*, 1983). The overdenture provides a simplified solution to a complex prosthodontic problem that is both reversible when growth and development demand that the prosthesis be altered and usually requires minimal intraoral modifications for its fabrication (Renner *et al.*, 1983).

The clinicians must balance treatment alternatives with the needs of the patient and parents. Treatment planning depends on various factors including: the family's financial limitations, the severity of AI, esthetic concerns, functional needs, and the status of patient's growth and development.

Treatment Outcome

By understanding the outcome of various restorative options for each AI phenotype, clinicians may select favorable approaches for AI patients. Proper diagnosis and application of treatment modalities that are specific to each individual patient with AI may enhance the treatment outcome. In addition, close follow-ups are essential achieving long-term success (Spair and Shapira, 2007).

Based on reported assessments of AI cases, it has been found that the treatment modalities of patients with AI vary, and their prognoses are generally unpredictable. Research on long-term follow up of restorative outcomes of AI patients is particularly scarce. Lindunger and Smedberg assessed the outcome of the prosthodontic management of adult AI patients and they found that 213 restorations in 15 patients were rated as acceptable to excellent, with one exception (Lindunger and Smedberg, 2005). The one exception was a crown that was considered unacceptable in all parameters, however, the reasons for failure were not provided. During the follow-up period, four (2%)

restorations had been recemented and 16 (8%) restorations had been remade. Five out of the 16 (2%) were remade because of porcelain fractures and 11out of the 16 (5%) were remade because of caries (Lindunger and Smedberg., 2005). The median age of the restorations was 60 months. Periodontal status in AI patients did not differ from patients without AI, but hypomineralized AI patients tend to have high scores in periodontal parameters. The overall results showed that the restorations performed well, and that all the patients had positive reactions to prosthodontic treatment. While this retrospective study has shown positive results of prosthodontic rehabilitation for patients with AI, research on long-term prognosis of restorative outcomes of AI patients is still particularly scarce and needs further investigations.

Psychosocial Impact

AI not only affects the patient's dentition but it can also have a significant impact on the psychosocial development of the patient. The first study that attempted to objectively characterize the psychosocial impact on AI patients was conducted by Coffield and colleagues. They found that subjects with AI had higher levels of social avoidance, distress and higher levels of dysfunction as well. The relationship of AI status to fear of negative evaluation, lower mastery and self-esteem was age-dependent. Additionally, subjects with AI tended to show an increase in mastery and self-esteem scores with age (Coffield *et al.*, 2005). One can speculate that AI patients could have had comprehensive dental treatment that helped them cope with their condition. In a retrospective study, Lindunger and Smedberg stated that all AI patients had positive reactions to their prosthodontic treatment (Lindunger and Smedberg, 2005). Interestingly, nearly half of

AI patients preferred restorative treatment done before the age of 16 (Lindunger and Smedberg, 2005). Therefore, it can be argued that early diagnosis and timely intervention may increase psychosocial health and self-esteem of AI patients, especially in the critical pre-adolescent and adolescent stages. The importance of dental esthetics, psychological and functional factors must also be considered when devising a treatment approach.

Objectives

The objectives of this study were to evaluate the outcome of various treatment modalities for patient with AI at the mixed dentition stage, to determine the oral health status of patients with AI who received treatment at the mixed dentition stage, and to determine patients' satisfaction with regards to appearance, function, and sensitivity post-treatment.

Chapter II

Manuscript

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage

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Running Head: amelogenesis imperfecta dental treatment assessment

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Abstract

Purpose: The purpose of this study was to assess the outcomes of restorative treatments of patients with amelogenesis imperfecta (AI) in the mixed dentition, to determine patients' oral health status post-rehabilitation, and to evaluate patients' satisfaction post-rehabilitation.

Method: A total of 74 restorations in 8 subjects with AI met the inclusion criteria. A recall visit was scheduled for conducting evaluations on restored teeth: their clinical status (based on modified U.S. Public Health Service criteria) and periodontal evaluations (gingiva index, plaque index, and pocket depth), as well as taking clinical photographs and radiographs. Subjects were asked to answer a survey regarding their self-assessment in esthetics, function, and sensitivity.

Result: Among the 74 restorations placed, 67 of these were present at the time of evaluation including: 31 posterior restorations (27 stainless steel crowns, 4 amalgams) and 36 anterior restorations (21 direct restorations (composite strip crowns, less than 4-surface composite resin restorations), and 15 indirect restorations (lab-fabricated resin veneers, lab-fabricated composite resin or acrylic crowns)). The remaining 7 restorations were lost. Ten restorations were rated as clinically unacceptable and therefore failure. The direct restoration group had a high number of unacceptable restorations (6/10). The need for retreatment was frequent in the direct restoration group (7/23). Periodontal evaluation showed that teeth with stainless steel crown had a moderate score in gingival index (mean= 2.3; SD=0.69) and in plaque index (mean=2.0; SD=0.92). Bleeding on probing was observed in every restoration group (stainless steel crown=20/23; amalgam=1/4; direct restoration=12/17; indirect restoration=14/15). PDL widening and

pulp canal obliteration were the common radiographic findings, however, these do not require clinical interventions but periodic evaluations. There was a statically significant difference in subjects' satisfaction on esthetics ($p=0.002$) and on sensitivity ($p=0.025$ while brushing; $p=0.010$ while eating) of their teeth post- rehabilitation.

Conclusions: During the mixed dentition stage, teeth affected with AI may be restored with conventional treatment modalities. Direct restorations may be successful as interim restorations and multiple repair and replacements have to be expected in the direct restoration group. Gingival inflammation and plaque accumulation were observed following restorative treatment of AI patients. Patients with AI were satisfied with their appearance and reported a decrease in sensitivity of their teeth after restorative treatment.

Keywords: amelogenesis imperfecta, mixed dentition, restorations, outcome assessment, patients' satisfaction

Introduction

Amelogenesis imperfecta (AI) is a hereditary defect of enamel affecting both the primary and permanent dentition.[1] It is a clinically and genetically diverse group of conditions caused by mutations in genes critical for normal enamel formation, mineralization, and maturation. The formation of enamel is a multistep process, and enamel defects can occur at any one of those steps. By definition, AI includes only those cases where enamel defects occur in the absence of other syndromes or metabolic disorders.[1] The incidence of AI ranges from 1 in 718 to 1 in 14,000 depending on the population studied.[1,2] Changes in color, thickness, hardness, and smoothness have been observed in the enamel of teeth affected by AI, depending on the type and severity of the disorder.

According to Witkop, AI can be classified as hypoplastic, hypomaturation, hypocalcified, and hypomaturation-hypoplastic with taurodontism.[1] In hypoplastic AI, the teeth are yellowish brown in color, rough in texture, and widely spaced. In hypomaturation AI, the clinical crowns are of normal size and contact adjacent teeth, but the mottled, brown-yellow enamel is soft. In hypocalcified AI, the enamel layer may be of normal thickness, but is rough and soft and wears away quickly following tooth eruption. In hypomaturation-hypoplastic AI with taurodontism, the enamel is mottled white-yellow-brown in color and is thin at the areas of hypomaturation. The permanent molars associated with this condition have taurodontism. In addition, other teeth may also have enlarged pulp chambers.[1]

AI affects the enamel crystallites formation resulting in abnormal crystallite morphology. [3,4] The decreased mineral content associated with the increased protein

content in AI enamel could affect the ability of these teeth to adequately bond to adhesive dental materials.[5-7] The high failure rate of composite resin bonding on AI teeth could be due to factors such as bonding failure or cohesive failure occurring at enamel, DEJ, or dentin level.

A variety of clinical implications may also be present, such as low caries susceptibility, rapid attrition, excessive calculus deposition, and gingival hyperplasia.[8,9] Anterior open bite is also a common finding associated with AI.[8,10] The severity of clinical problems varies with each type of AI. Low caries susceptibility has been reported in children with severe hypoplastic and hypomineralized AI.[11] While Sundell stated that the bacteriological and salivary data in the AI patients were inadequate to explain the low caries susceptibility[11], it was suggested that additional investigations which focus on determining the difference of oral microflora between affected and unaffected individuals would be informative. Non-enamel-related manifestations may also occur including accelerated dental development,[8,12] high prevalence of dental impaction,[12,13] congenital missing teeth,[13] crown and/or root resorption,[8,13] pulp calcification,[8,13] and associated abnormalities.[8-10, 12,13] The presence of these abnormalities has apparent implications on the clinical management of these patients.

Often these patients experience concern over poor esthetics, tooth sensitivity, difficulty in maintaining oral hygiene, decreased masticatory function, and a lower self-esteem, which all affect their over-all quality of life.[14] As a result, most AI patients require extensive dental treatment, which can be time consuming and pose a significant economic burden on their family. Treatment of AI depends on the individual diagnosis and phenotype. Proper diagnosis and awareness of the different treatment modalities in

individual cases of AI may favorably influence the treatment outcome. Treatment options have been advocated in the literature, including the use of glass ionomer cements, composite resins, stainless steel crowns, lab-fabricated crowns, and even multiple extractions necessitating an over denture.[10,15,16,17,18] The optimal patient management must take into consideration the phases of dental development since treatment needs may differ in the primary, mixed dentition or permanent dentition.[19]

In the mixed dentition stage, the treatment goals are to preserve tooth structures, to maintain vitality, decrease tooth sensitivity, establish correct interproximal and occlusal function, and improve esthetics. However, rehabilitation in the mixed dentition is complex, since teeth have different eruption sequence and definitive treatment cannot be rendered until the complete of eruption of the permanent dentition. In conjunction with treatment, strict oral hygiene instruction and preventive treatments are essential in order to prevent caries, gingivitis and calculus formation which may exacerbate existing problems.

AI not only affects the patient's dentition, but it can also have a significant impact on the psychosocial development of the individual.[14] AI patients reported being teased about their teeth and being unhappy with the color, shape, and size of teeth when compared to the unaffected patients. In a retrospective study, Lindunger and Smedberg assessed the outcome of restorative treatment and stated that all AI patients were positively influenced by their restorative treatment and nearly half of the patients preferred restorative treatment done at an earlier age.[20] Therefore, dental treatments may not only preserve the tooth structure, improve function, and reduce tooth sensitivity but these may also improve psychosocial well-being of AI patients, especially in the critical

pre-adolescent and adolescent stages. The importance of dental esthetics, psychological and functional factors must also be considered when developing a treatment approach.

By understanding the outcome of various restoration alternatives for each type of AI, clinicians may select more favorable approaches for each individual AI patient. Unfortunately, research on the long-term follow up of restorative outcomes of patients with AI is particularly scarce. The majority of the evidence relies on case reports that present treatment modalities and outcomes of only a few AI patients with or without an additional description of their family members. It is surprising to note that there is currently no standard of care established for managing patients with AI, especially during the mixed dentition stage.

The purpose of this study was to evaluate the outcome of various treatment modalities for patient with AI at the mixed dentition stage, to determine the oral health status of patients with AI who received treatment at the mixed dentition stage, and to determine patients' satisfaction with regards to appearance, function, and sensitivity post-treatment.

Methods

This study was approved by the University of Michigan Medical School the Institutional Review Board, Ann Arbor, Michigan. The subjects were recruited from the patient population of the Graduate Pediatric Dentistry Clinic at the University of Michigan, School of Dentistry.

The data was collected between October 2, 2009 and August 23, 2010. Twenty-nine patients identified with AI in the electronic health record (MiDent) system were considered as potential candidates. Twelve candidates met the following inclusion

criteria to be qualified: 8-18 years of age with AI and no other systemic disorders and a history of restorations placed on the permanent first molars and the permanent incisors at least 6 months ago. Their parent or legal guardian was introduced to this study by phone. Written informed consent was obtained from the parent or legal guardian and assent were obtained from children on the day of dental recall appointment. Eight subjects consented to this study.

Procedure. A recall appointment was scheduled for the purpose of conducting evaluations on restored teeth: their clinical status (based on modified U.S. Public Health Service criteria) and periodontal evaluations (gingiva index, plaque index, and pocket depth), as well as taking clinical photographs and radiographs. At the end of the appointment, subjects were asked to answer a survey regarding their self-assessment in esthetics, function, and sensitivity.

Two research investigators, a pediatric dental resident and an attending pediatric dentist, performed the evaluations. When disagreement occurred, they re-evaluated all photos, radiographs, and teeth in order to reach a consensus. All the analysis was based on consensus.

Material. The parent consent, subject assent, and HIPAA forms were written according to IRB guidelines. Intraoral photographs (taken with a digital single-lens reflex camera) were used to evaluate the color and texture of teeth and gingivae. An attempt was made to take 15 intraoral photographs. In some cases, only 5 photographs were taken due to behavior issues. Restorations were evaluated based on the modified U.S. Public Health Services (USPHS) criteria. A blunt explorer with tip of 400 μm was used to assess restorations on the permanent first molars and permanent incisors. The

following characteristics were selected depending on types of restoration: surface, color match, anatomic form, margin integrity/ adaptation, fracture restoration, caries, and wear. The periodontal status was determined by assessing the modified Quigley-Hein plaque index (TQHPI; Turesky 1970), modified gingiva index, pocket depth, and bleeding on probing on the permanent first molars with restorations and permanent incisors with restorations. To evaluate any pathology, a total of 10 radiographs were taken using the Rinn system for alignment. If recent radiographs were available, additional study radiographs were not taken. Subjects were asked to answer a survey with 10 questions regarding their opinions about their smile, esthetics of their teeth, function, and sensitivity before and after restorative treatments. The Wong-Baker face pain-rating scale was modified and used to facilitate the subject's self-reported treatment outcome.

Statistical analysis. Data was analyzed using the Statistical Package for Social Sciences (SPSS Inc.,Version 17.0, Chicago, IL). Descriptive statistics summarized the findings. Mixed model analysis was used to compare the periodontal status in the direct restoration and indirect restoration group, to control for multiple teeth per subject. Paired t-test was used for comparing survey responses. Results with a p-value of less than or equal to 0.05 were considered statistically significant.

Results

Data were collected from 4 hypoplastic, 2 hypocalcified, and 2 hypoplastic-hypomaturation AI subjects (N=8; 6 females/ 2 males; age range =9.4 years ~ 15.9 years old). The subtypes of AI were distinguished based on clinical characteristics and radiographic features. Among the 8 subjects, 6 subjects completed the research

procedures. One of the remaining subjects completed all research procedures but the survey because he was undergoing dental treatment on other teeth, while the other refused to participate in the clinical evaluation of restorations and periodontal examination.

The initial chart review identified 8 AI patients with 96 affected teeth. Among 96 teeth, 22 teeth were excluded (20 teeth without restorations, 1 missing tooth due to previous extraction, and 1 less than 6-month old direct restoration). Table 1 provides an overview of the subject demographic data and the restorations they received. The 74 remaining teeth were restored and classified into 4 different groups, based on the type of material used. Of the 74 remaining teeth, 67 restorations were present. Among these 67 restorations, there were 27 stainless steel crowns, 4 amalgams, 21 direct restorations, and 15 indirect restorations in 8 subjects. Seven restorations were lost and therefore were not evaluated. Among 7 lost restorations, 6 were direct restorations and 1 was indirect restoration. In this study, the direct restoration group included composite resin strip crowns and fewer than 4-surface composite resin restorations. Amalgam did not include in the direct restoration group. The indirect restoration group included lab-fabricated resin veneers and lab-fabricated composite resin or acrylic crowns.

Table 2 provides a summary of the distribution of the types of restoration received as well as the age range when restorations were first placed. The mean age of the present restorations was 38.53 months with a range of 6 to 100 months. The median post-placement-time of stainless steel crown was 27 months while direct restoration group had a median post-placement-time of 41 months.

Table 3 shows the results of clinical evaluation of restorations. Of the total 67 teeth evaluated, only 59 restorations were evaluated clinically due to subject participation.

The results of clinical assessment of restorations revealed 10 restorations were rated as unacceptable and therefore failure, the highest being in the direct restoration group (N=6). The stainless steel crown group had 1 out of 23 restorations with wear/crown perforation and the amalgam group had 1 out of 4 restorations with rough surface. The indirect restoration group had 2 out of 15 restorations with unacceptable margin.

Table 4 provides the summary of clinical restorations failures. With the inclusion of these 6 lost direct restorations, the failure rate of the direct restoration group increased (12/23). The failure rate of the indirect restoration group did not increase as much with addition of the one lost indirect restoration. In addition, the need for retreatment was frequent in the direct restoration group. A total of 11 restorations required retreatment, including 3 stainless steel crown replacements, 7 direct restoration repairs, and 1 indirect restoration recementation.

A total of 59 teeth with restorations in 7 subjects were examined for periodontal status due to subject participation. Teeth that received stainless steel crown had a moderate score in gingival index (mean= 2.3; SD=0.69) and in plaque index (mean=2.0; SD=0.92). Using the mixed model analysis to compare the direct restoration group and indirect restoration group, statistically significant differences were found in pocket depth in the indirect restoration group ($p=0.000$) and in plaque index in the direct restoration group ($p=0.024$). Bleeding on probing was observed in every restoration group (stainless steel crown=20/23; amalgam=1/4; direct restoration=12/17; indirect restoration=14/15).

Sixty-seven teeth with restorations in 8 subjects were evaluated radiographically. There were no furcation or apical radiolucencies observed in any group. Margin discrepancy (9/27) was observed only in the stainless steel crown group. In addition,

crown-tooth size discrepancy (6/27) was observed in stainless steel crown group. PDL widening (N=8) and pulp canal obliteration (N=5) were common radiographic findings and these required no clinical interventions but periodic evaluations.

Table 5 shows the results of survey. The 10 survey questions regarded the subjects' satisfaction with the esthetics, function, and sensitivity of their teeth. One subject did not answer post-treatment questions due to dental treatment in progress. Although differences were noted in smiling (p=0.140) and eating regular food (p=0.93), no statistical difference was found before and after treatment. There were statistically significant differences in subjects' satisfaction on esthetics (p=0.02) and on tooth sensitivity while brushing (p=0.025) and eating (p=0.01) post-rehabilitation.

Discussion

As expected, a majority of enrolled subjects in this study have a hypoplastic type of AI. This is in line with other studies showing hypoplastic AI accounting for 60-73% of cases evaluated.[21]

Stainless steel crowns were used to restore most the permanent molars with AI (27/31). Many case reports have suggested that stainless steel crown is the choice of cost-effective restoration for young permanent molar.[10,19] In this study, the majority of stainless steel crown were judged as clinically acceptable (22/23). Interestingly, 1 out of 23 stainless steel crowns was perforated. According to the record, this stainless steel crown had at least 52-month prior to its perforation. The perforation of the stainless steel crown may have happened between subject's last dental visit and the day of evaluation

because the subject did not keep up with the recommended recall visit for 3 years. It has also been shown in a retrospective study on children with AI that a 5-year survival rate for stainless steel crowns on permanent molars was 55%.[22] Due to single assessment of restorations, it is impossible to conduct a survival analysis in this study.

Margin discrepancy was determined based on evaluation of radiographs assessing whether or not restorations encroached on the biologic width of the tooth. Margin discrepancy (9/23), space between restoration margin and the alveolar bone, appears to be a concern with stainless steel crown restorations in this study. However, radiographs of maxillary teeth were challenging due to the presence of the palatal root, close vicinity of the developing permanent tooth germ and often deviated film angulations. This result must be interpreted with caution.

About 3mm space should be preserved from restoration margin to alveolar bone, allowing for 2mm of biological width and 1 mm of sulcus depth.[23] When the restoration margin is placed subgingivally, this could lead to insufficient space between restoration margin and alveolar bone. However, it is often inevitable to place a stainless steel crown margin placed subgingivally in young permanent molars. If the restoration margin is placed subgingivally, this may not only increase the risk of invading soft tissue attachment but also create a plaque-retentive area that stimulates more pronounced, plaque-induced inflammatory responses. Research indicated that clinically evident of gingivitis may be found in the presence of a stainless steel crown, especially when inadequate crown length, contour and position, or excessive cement remaining in the gingival sulcus were observed.[24]

In this study, the most commonly observed problem among stainless steel crown

restorations was crown-tooth size discrepancy. This showed that clinicians tend to choose the preformed stainless steel crown with a size that is smaller than the contour of the original tooth. This is understandable since the crown morphology of AI patients is already different from and often smaller than the crown morphology of patients without enamel defects; the cementoenamel junction of the clinical crown is often located subgingivally and difficult to discern due to thin or defective enamel. The crown contour may have significantly changed following tooth reduction, even without removing all defective enamel. This crown-tooth size discrepancy may have detrimental effects leading to open proximal contacts and exposure of tooth structure following progressive eruption of the tooth and its surrounding structures. With progressive eruption of tooth, it is difficult for patients to keep the margin of the restoration and the surrounding gingival tissues clean, hence, the restoration may fail.[21] Therefore, taking a periapical radiograph to ensure proper size and position of crowns after seating and prior to its cementation is recommended.

Amalgam was placed on four (4/31) permanent first molars. Teeth restored with amalgam are often not severely affected by AI and therefore can retain an intracoronal restoration, as was the case in one subject. The small sample size, however, prevented a meaningful statistical analysis of this restorative therapy.

Direct restoration (N=27) and indirect restorations (N=16) were mostly placed on the permanent incisors. Direct restorations are frequently placed on partially erupted incisors which may increase the difficulty in isolation and in margin placement. The direct restoration group had a high number of unacceptable restorations (N=6 in 4 categories). With the inclusion of 6 lost direct restorations, more than half of the direct restorations

were considered as a failure (12/23) when compared to other types of restoration. The high failure rate of the direct restorations may be due to bonding failure. As the bond between enamel and composite resin restorations is highly dependent on the enamel surface change after acid etching, Seow and Amaratunge concluded that typical etch patterns are generally not observed in the smooth hypoplastic and male X-linked variants of AI.[7] This conclusion may be one of the bonding failure reasons. On the other hand, reports in the literature suggested that a thin, nonprismatic enamel layer could be sufficient to retain bonded material adequately.[10,17,25] Other reasons for the failure of composite resin on teeth affected by AI could be due to factors other than bonding failure, such as cohesive failure occurring at the enamel, DEJ, or dentin level.

Though defective margins (radiographic evaluation=7/21; clinical evaluation=4/17) appears to be a concern in the direct restoration group, these can be easily repaired. While restorations with overhanging margin can be recontoured without replacing the current restorations, it is important for restorations with open margin or restoration fracture to be retreated. The current restorations may not necessarily have to be removed completely. Defective margins may also contribute to gingiva inflammation. It was also surprising to note that the indirect restoration group had a moderate score in pocket depth ($p=0.000$) when compared to the direct restoration group. One can speculate that indirect restorations may require subgingival margin preparations to achieve esthetics, therefore maintaining optimal oral hygiene in those areas can be a challenge.

The results in mixed model analysis indicated that when comparing the direct restoration group and the indirect restoration group, there was statistically significant difference in the plaque index in the direct composite group ($p=0.024$). This may suggest

that direct restoration had a greater degree of plaque accumulation making it difficult to maintain optimal oral hygiene. The nature of material, surface roughness and margin deficiencies of the direct restorations may also increase the chances for plaque accumulation.

Though bleeding on probing was observed in every restoration group (stainless steel crown=20/23; amalgam=1/4; direct restoration=12/17; indirect restoration=14/15), this result needs to be read with caution since bleeding on probing is often used to monitor the changes over time. Therefore the single assessment of bleeding on probing may not be meaningful.

PDL widening and pulp canal obliteration were common radiographic findings. However, without baseline radiographs for comparison, we could not conclude that PDL widening and pulp canal obliteration were a result of the restoration itself. There is no report on radiographic changes of AI patients before and after restorative treatment in the literature.

This study was in agreement with the Lindunger and Smedbergs' study, finding that restorations had a positive influence on patients with AI.[20] There was, however, little improvement in chewing function. Two subjects (2/8) reported that there was no improvement with chewing function before or after restorative treatment. We speculate that following restorative treatments, although reported to have a better chewing function, AI patients may still have to be selective with proper food types to ensure adequate biting, chewing and to minimize discomfort and to prevent any injury to their existing restorations. This result, though from only 8 subjects, provided a statistically significant evidence, suggesting the importance of restoring teeth with AI to improve esthetics and

reduce tooth sensitivity. Similarly, restorations are important in improving subjects' self-perception. Therefore, as Coffield *et al*., have suggested, dental treatments could be medically necessary for patients affected with AI.[14]

There were limitations to the current study and its conclusions should be taken with caution. First, due to the specific study objective, and the particular stage of treatment being assessed, the number of subjects recruited for this study was very small. In addition, there was no comparable control group available. Second, these restorations were evaluated at one time point only. No baseline data was available, therefore it was impossible to know how changes took place over time. Third, these 59 restorations were from only 7 subjects. Therefore, it is not possible to conduct statistical analyses on the clinical, radiographic and periodontal outcomes obtained from 4 different types of restoration placed on teeth affected by 3 different types of AI. With this small of a sample, the authors could not investigate the impact of the severity of AI phenotype on the different types of restoration. Potential limitations of our survey may include that subjects' answers to the survey questions which were applicable before and after treatment, were given at the same time. Subjects may have forgotten what they really felt before the treatment.

Further research into several aspects is required to strengthen this study. Comparisons of the oral health status before and after restorative treatment of patients with different variants of AI will enable determination of effectiveness of the specific restorations for each type of AI. Furthermore, studies of qualitative and /or quantitative change of the saliva would provide important insight into the cause of periodontal problems in AI patients. Also, researchers may evaluate restorations at fixed time points

and conduct a survival analysis in order to gain information on durability and sustainability of restorations.

Conclusions

Based on this study's results, the following conclusions can be made:

1. During the mixed dentition stage, teeth affected with AI can be restored using conventional treatment modalities. Direct restorations, such as composite resin strip crown and fewer than 4-surface composite resin restoration, had a high percentage of unacceptable and failed restorations (12/23). They should be considered 'interim restorations' and multiple repairs and replacements have to be expected. Periodic maintenance will be necessary to keep such interim direct restorations intact and functional.
2. Gingival inflammation and plaque accumulation were observed following restorative treatment of patients with AI.
3. Patients with AI were satisfied with their appearance, and expressed a decrease in tooth sensitivity when eating and brushing their teeth after restorative treatment.

Acknowledgements

We like to thank the staff and patients of Children Dental Clinic in the University of Michigan for their support of this study and Miss Angela Menighini, research assistant, for her help in recruiting subjects. We also like to thank Ms. Kathy Welch at the University of Michigan Center for Statistical Consultation and Research for her help and guidance in data analyses. This research was supported by a grant from the Delta Dental Foundation of Michigan and Rackham Graduate Fund.

Table 1: Demographic Data of Subjects (N=8) and the Restorations (N=75) They Received on Their Teeth

Subject	AI type[1]	Sex	Age	Type of restoration				Missing[3]	No restoration[4]
				Stainless steel crown	Amalgam	Direct restoration[2]	Indirect restoration		
1	1	F	13y7m	4	0	8	0	0	0
2	2	F	12y5m	4	0	4	0	0	4
3	1	F	15y9m	4	0	8	0	0	0
4	1	M	15y7m	4	0	2	4	0	2
5	2	F	9y4m	4	0	2	0	0	6
6	3	M	13y2m	4	0	0	0	0	8
7	3	F	14y	1	3	0	8	0	0
8	1	F	15y	2	1	4	4	1	0
Total				27	4	28	16	1	20

[1] AI type: 1= hypoplastic AI; 2= hypocalcified AI; 3=hypocalcified- hypomaturation AI
[2] The age of one direct restoration was less than 6-month old thus was excluded.
[3] One missing tooth was excluded.
[4] Twenty teeth without restorations were excluded.

Table 2: Summary of Restoration (N=67) and Tooth Type Evaluated with Age of Placement Calculated[1]

Type of restoration	Tooth type	AI1[2]	AI2[3]	AI3[4]	Total	Restoration age (months)				
						Mean	Std. deviation	median	minimum	maximum
Stainless steel crown	Molar	14	8	5	27	49.33	35.60	27.00	9	100
Amalgam	Molar	1	0	3	4	13.00	3.46	11.00	11	17
Direct restoration	Incisor	17	4	0	21	45.29	28.32	41.00	9	81
Indirect restoration	Incisor	7	0	8	15	14.73	14.68	8.00	6	43

[1] A total of 67 restorations were present at the day of evaluation. Not included were 7 lost restorations and one direct restoration less than 6-month old.
[2] AI1= hypoplastic AI
[3] AI2= hypocalcified AI
[4] AI3=hypocalcified- hypomaturation AI

Table 3: Clinical Evaluation of Restorations (N=59)[1,2]

Type of restoration (Number)	Surface		Color		Form		Margin		Fractures		Caries		Wear		Total score	
	A	U	A	U	A	U	A	U	A	U	A	U	A	U	A	U
Stainless steel crown[3] (23)	n/a		n/a		n/a		23	0	n/a		23	0	22	1	22	1
Amalgam[3] (4)	3	1	n/a		4	0	4	0	4	0	4	0	n/a		3	1
Direct restoration[3] (17)	15	2	17	0	15	2	13	4	17	0	16	1	n/a		11	6
Indirect restoration[3] (15)	15	0	15	0	15	0	13	2	n/a		15	0	15	0	13	2
Total (59)	33	3	32	0	34	2	53	6	21	0	58	1	37	1	49	10

[1] Based on the modified U.S. Public Health Service criteria. Restorations were rated as "A" if they received every score in the acceptable range. Restorations were rated as "U" if they had a score in any of unacceptable range.

[2] Fifty-nine restorations were evaluated. One subject (4 stainless steel crowns and 4 direct restorations) did not participate in clinical evaluation.

[3] n/a= not applicable

Table 4: Summary of Clinical Restorations Failures (N=66)[1]

Type of restoration	Number of teeth	Lost Restoration[2]	Unacceptable Restoration[3]	Total failure
Stainless steel crown	23	0	1	1
Amalgam	4	0	1	1
Direct restoration	23	6	6	12
Indirect restoration	16	1	2	3
Total	66	7	10	17

[1] Sixty-six teeth were evaluated including: 59 teeth with restorations and 7 teeth that lost restorations.
[2] Lost restorations were based on initial chart review.
[3] Unacceptable restorations were based on clinical evaluation of restorations

Table 5: Outcome of Survey (N=8)[1]

		Mean[2]	Paired t-test p-value
Do you smile for pictures?	Before treatment	2.43	.140
	After treatment	1.71	
Do you like the way your teeth look?	Before treatment	4.43	.002[3]
	After treatment	1.57	
Are you able to eat regular food?	Before treatment	3.71	.093
	After treatment	2.43	
How sensitive are your teeth? During tooth brushing	Before treatment	3.00	.025[3]
	After treatment	1.67	
How sensitive are your teeth? When eating	Before treatment	3.29	.010[3]
	After treatment	1.71	

[1] One subject did not answer after treatment questions due to treatment in progress.
[2] On a scale of five, subjects indicated their answer to each question from 1 (best) to 5 (worst) subjectively.
[3] Denotes statistical significance ($p<0.05$)

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Chapter III

Extended Materials

Extended Methods

This study was approved by The University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board for Human Subject Research in Ann Arbor, MI (HUM00027771, Appendix A). The subjects were recruited from the patient population of the Graduate Pediatric Dentistry Clinic at the University of Michigan, School of Dentistry. Twenty-nine subjects identified with AI in the electronic health record (MiDent) system were considered as potential candidates. Twelve candidates met the following criteria to be qualified: 8-18 years of age with AI and no other systemic disorders; a history of restorations placed on any of the permanent incisors and permanent first molars at least six months ago. The parent or legal guardian was introduced to this study by phone (Appendix B). They were given a description of the study steps with freedom to drop out at any time. Monetary compensation/ gift card would still be rewarded regardless of whether or not the subject completed the study. If parent/guardian and the subject both agreed to participate in the study, the study procedures were then scheduled concurrently with a dental recall appointment. Written informed consent was obtained from the parent/guardian and written assent was signed by the subject-patient (Appendix C, D, and E). Eight subjects consented to this study.

Two research investigators, a pediatric dental resident and an attending pediatric dentist, performed all the evaluations. Calibrations and training sessions for the

evaluators were conducted with the help of an additional pediatric dentist. When disagreement occurred between these two investigators, they re-evaluated all photos, radiographs and teeth to reach a consensus.

On the day of the appointment, an initial review of the subjects' dental records was conducted to collect clinical diagnosis, treatment rendered, and treatment notes (Appendix F). The subjects' current radiographs from their records were also assessed. When supplementary information was needed for the radiographic evaluation, additional study radiographs were taken at the same appointment. The research procedures included clinical evaluations and periodontal evaluations on restored teeth, as well as taking clinical photographs and radiographs. At the end of the appointment, subjects were asked to answer a survey regarding their self-assessment in esthetics, function, and sensitivity.

Clinical Evaluation of Restorations

Intraoral photographs (taken with a Nikon D70 digital single-lens reflex camera, mirror and cheek retractors) were used to evaluate the color and texture of teeth and gingiva. An attempt was made to take 15 intraoral photographs. In some cases, only 5 photographs were taken due to behavior issues. The 15 intraoral photographs included: 2 occlusal views of the full maxillary and mandibular arches, 1 frontal view of the anterior teeth in occlusion, 2 facial views of the anterior teeth, 4 lateral views of the molars, and 6 lingual views of either the molars or the anterior teeth. If subjects were only able to tolerate 5 intraoral photographs, the views were limited to: 1 frontal view of the anterior teeth in occlusion, 2 lateral views of the molars in occlusion, and 2 occlusal views of the full maxillary and mandibular arches.

A blunt explorer with tip of 400 μm was used to assess restorations on the permanent first molars, central incisors, and lateral incisors. Restorations were evaluated based on the modified U.S. Public Health Service (USPHS) criteria (Cvar JF & Ryge G 1971) (Appendix G, H, and I). Characteristics were selected depending on types of restoration: surface, color match, anatomic form, margin integrity/ margin adaptation, fracture restoration, caries and wear. Each characteristic was given a score. A score 0 indicated that the quality of restoration fulfilled the high standard of criteria and was acceptable. A score 1 indicated that the quality of restoration fulfilled the moderate standard of criteria and was acceptable. A score 2 indicated that the quality of restoration did not fulfill criteria and was unacceptable (Appendix G, H, I). If a restoration received a score that rated it as unacceptable in any characteristic category, this restoration was rated as unacceptable. Four types of restoration were evaluated in this study including: stainless steel crown, amalgam, direct restoration, and indirect restoration. Amalgam did not include in the direct restorations group. Direct restoration included composite resin strip crown or fewer than 4-surface composite resin. Indirect restoration included lab-fabricated resin veneers and lab-fabricated composite resin or acrylic crowns.

Periodontal Evaluation

A periodontal probe (Hu-Friedy 23 QW Expros) was used to assess the periodontal health status on teeth with restorations. The periodontal health status was determined by assessing the modified gingival index (Appendix J), the modified Quigley-Hein plaque index (TQHPI; Turesky 1970) (Appendix K), pocket depth, and bleeding on probing (Ainamo & Bay 1975) on the permanent first molars, central incisors, and lateral incisors

(Appendix L).

Radiographic Evaluation of Restorations

The Rinn system was used to obtain standardized radiographs. A total of ten radiographs were taken to determine the level of alveolar bone crest in relation to the restoration margin as well as any pathological findings such as furcation radiolucency, apical radiolucency, PDL widening, and fractures of tooth structure (Appendix M). These 10 films consisted of four posterior periapical films, three upper incisors periapical films, and three lower incisors periapical films. If recent radiographs were available, additional study radiographs were not taken.

Survey

At the end of the appointment, subjects were asked to answer a survey with 10 questions regarding their opinions about their smile, esthetics of their teeth, function and sensitivity before and after restorative treatments (Appendix N). The Wong-Baker face pain-rating scale was modified and used to facilitate the subjects' self-reported treatment outcome. Subjects indicated their answer to each question on a scale of 5, 1 being the best and 5 being the worst.

Statistical Analysis

Data was analyzed using SPSS (Version 17.0, Chicago, IL). Descriptive statistics were used to summarize findings. Mixed model analysis was used to compare the

periodontal status in the direct restoration and indirect restoration group, to control for multiple teeth per subject. Paired t-test was used for comparing survey responses. Results with a p-value of less than or equal to 0.05 were considered be statistically significant.

Extended Results

One pediatric dental resident and one attending faculty member at the University of Michigan evaluated those eight subjects. The initial inter-rater agreement was determined using Cohen's Kappa Method. The level of agreement was determined to be between fair and good in caries category of clinical evaluation (Kappa=0.664)**.** The level of agreement was determined to be poor in margin category of clinical evaluation (Kappa= -0.124). When the disagreement occurred, both raters re-evaluated all photos, radiographs (Appendix O), and teeth in order to reach a consensus. All the analysis was based on consensus.

Demographics

A total of 8 subjects with an age range of 9 years 4 months to 15 years 9months old, with 2 males and 6 females, met the inclusion criteria and consented to this study. Among the 8 subjects, 4 subjects had hypoplastic AI, 2 had hypocalcified AI and 2 had hypoplastic-hypomaturation AI. The subtypes of AI were distinguished based on clinical characteristics and radiographic features. Among the 8 subjects, 6 subjects completed the study procedures. One of the remaining subjects completed all study procedures but the survey because he was undergoing dental treatment on other teeth, while the other refused to participate in the clinical evaluation of restorations and periodontal examination.

Table 1 provides an overview of the subject demographic data and the restorations they received. A total of 96 teeth were initially reviewed by the primary investigator. Among 96 teeth, 22 teeth were excluded (20 teeth without restorations, 1 missing tooth

due to previous extraction, and 1 less than 6-month old direct restoration). Of the 74 remaining teeth, the 7 restorations were lost therefore were not evaluated. Of these lost restorations, one was an indirect restoration and six were direct restorations. Six of these seven teeth continued to be only observed due to lack of symptoms or multiple repair failures. One missing direct restoration was scheduled for repair. Of the remaining 67 restorations evaluated, only 59 restorations were evaluated clinically due to subject participation. One subject refused to participate in clinical or periodontal evaluations representing 4 stainless steel crowns and 4 direct restorations. Figure 1 shows the distribution of teeth.

Summary of restoration and tooth type

Table 2 provides the distribution of the types of restoration received as well as the age range when restorations were first placed. Sixty-seven restorations with four types of restoration were evaluated. The stainless steel crown group made up the largest number of restorations (N=27) followed by the direct restoration (N=21), the indirect restoration (N=15), and the amalgam group (N=4). Stainless steel crowns and amalgam were placed on the permanent molars. Direct restoration and indirect restorations were placed on the permanent incisors. The mean age of the present restorations was 38.53 months with a range of 6 to 100 months. The median post-placement-time of the stainless steel crown group was 27 months while the direct restoration group had a median post-placement-time of 41 months.

Clinical Evaluation of restorations

Table 3 shows the results of clinical evaluation of restorations. Because subject 2 did not participate in the clinical evaluation of restorations, 59 teeth with restorations in 7 subjects were evaluated. The results of clinical assessment of the restorations revealed that 10 restorations were rated as unacceptable and therefore failure, the highest being in the direct restoration group (N=6). The direct restoration group had six unacceptable restorations (6/17) in 4 categories including surface roughness (N=2), unacceptable form (N=2), defective margin (N=4) and caries development (N=1). Three unacceptable direct restorations presented with more than one unacceptable category. The stainless steel crown group had one unacceptable restoration (1/23) with crown/wear perforation and the amalgam group had one unacceptable restoration (1/4) with a rough surface. The indirect restoration group had two unacceptable defective margins (2/15).

Table 4 summarizes clinical restoration failures distinguished by the type of restoration. The seven lost restorations were included in this table though they are not evaluated clinically. With the inclusion of these 6 lost direct restorations, the failure rate of the direct restoration group increased (12/23). The failure rate of the indirect restoration group did not increase as much as with the addition of one lost indirect restoration (3/16).

Table 5 shows the frequency of retreatment among different types of restoration. A total of 11 restorations required retreatment including: 3 stainless steel crown replacements, 7 direct restoration repairs, and 1 indirect restoration recementation. The reasons for replacing stainless steel crown were cement failure or perforated crown. Due to the partial fracture of direct restoration, 7 direct restorations needed composite resin

repair. The earliest repair was 2-month after the first placement of the restoration in the direct restoration group. Six direct restorations were repaired at least twice each. One subject with 4 indirect restorations was especially interesting. Though all 4 teeth underwent a crown-lengthening procedure prior to crown preparation, one indirect restoration required recementation 2 weeks following its initial placement. Unfortunately, this recemented indirect restoration was lost after the second recementation. Instead of replacing the indirect restoration, composite resin was placed to cover the tooth structure.

Periodontal evaluations

Table 6 shows the results of periodontal health status. A total of 59 teeth with restorations in 7 subjects were evaluated due to subject participation. Fifty-one teeth with restorations had a gingival index of at least 1, signifying the presence of gingival inflammation (51/59). Teeth that received stainless steel crowns had a moderate score in gingival index (mean= 2.3; SD=0.69). Seven direct restorations (7/17) had a gingival index score equal to or greater than 3. A gingival index score greater than or equal to 3 indicates severe gingival inflammation. Teeth that received stainless steel crowns had a moderate score in plaque index (mean=2.0; SD=0.92). Six stainless steel crowns (6/23) have a plaque index score equal to or greater than 4. A plaque index score equal to or greater than 4 indicates severe plaque accumulation. Teeth that received indirect restorations had a moderate score in pocket depth (mean= 2.10; SD=0.20). Three stainless steel crowns (3/23) had a pocket depth score equal to or greater than 4mm. Among these 3 stainless steel crowns, two were from the same subject. These two restorations also had a high score in plaque index (PI=4.0) and in gingival index (GI=3.5).

Using the mixed model analysis to compare the direct restoration group and the indirect restoration group, statistically significant differences were found in pocket depth in the indirect restoration group (p=0.000) and in plaque index in the direct restoration group (p= 0.024).

Bleeding on probing was observed in the stainless steel crown (20/23), the amalgam (1/4), the direct restoration (12/17) and the indirect restoration group (14/15).

Radiographic evaluation of restorations

Table 7 shows the findings of radiographic evaluation. Sixty-seven teeth with restorations in 8 subjects were evaluated. There were no furcation or apical radiolucencies observed in any group. PDL widening was observed in 8 restorations total, none of which were from the amalgam group. Pulp canal obliteration was observed in 5 restorations total, none of which were from the indirect restoration group. None of these restorations was considered failure based on the radiographic findings. The direct restoration group also had numbers of restorations with overhang margin (4/21) and open margin (3/21). Margin discrepancy (9/27) was only observed in the stainless steel crown group. In addition, crown-tooth size discrepancy was observed in the stainless steel crown (6/27) and the direct restoration group (1/21).

Outcome of survey

Table 8 shows the survey questions and results. The 10 survey questions regarded the subjects' satisfaction with the esthetics, function, and sensitivity of their teeth. One subject did not answer post-treatment questions due to dental treatment in progress. A

paired t-test analysis of the subjects' self-assessment before and after the placement of restorations indicated a statically significant difference in subjects' satisfaction on esthetics (p=0.02) and on sensitivity of their teeth while brushing (p=0.025) and eating (p=0.010) after the placement of restorations.

Although differences were noted in smile and in eating regular food, there was no statistical difference before and after treatment. When subjects were asked whether they smile for pictures, they reported being able to smile after the placement of restorations (mean=2.43 versus mean=1.71, p=0.140). When subjects were asked whether they are able to eat regular food (e.g. meat, ice cream, juice, corn on the cob), they reported being able to eat regular food after the placement of restorations (mean= 3.71 versus mean=2.43, p=0.93).

Extended Discussion

AI is a hereditary enamel defect manifesting in poor dental esthetics and sensitivity that frequently requires extensive dental treatment. In addition, AI has a significant impact of the psychosocial development on the affected individuals (Coffield *et al.,* 2005). Conventional treatment approaches using partial or full coverage restorations have been successful in reconstructing the affected dentition. However, significant cost, multiple retreatments and frequent dental visits compromise many patients' compliance. By understanding the treatment outcome of various restorations, clinicians may select appropriate treatment approaches in order to improve esthetics, function, and to reduce tooth sensitivity.

In this study, 74 restorations in four restorative modalities were evaluated. As shown in table 3, 10 restorations were rated as unacceptable and therefore failed based on clinical evaluations. Including the 6 lost direct restorations, the direct restoration group had a high ratio of unacceptable and failed restorations (12/23). Although the indirect restoration group had 3 unacceptable and failed restorations (3/16), the mean age of these restorations were only 14 months versus 45.29 months for the direct restoration group. Therefore, it cannot be concluded that the indirect restoration group performed better than the direct restoration group.

Direct restorations (N=27) and indirect restorations (N=16) were mostly placed on incisors. One interesting observation was that younger patients tended to have composite resin restorations while older patients often have lab-fabricated crowns or veneers on incisors. The explanation for this observation is that older patients have their teeth and

the contour of these supporting structures are stabilized and closed to their final positions. The length of the clinical crown due to eruption allows for better retention of the full coverage restoration and also the pulp has receded and less chance for pulp exposure occurs when restoring teeth with full coverage crowns.

Subject eight (age 15) had one molar extraction, which was performed before the subject was referred to our clinic. In addition, one of her molars had root canal therapy to treat pulpitis after the tooth reduction for stainless steel crown placement. Because of thin enamel and relatively large pulp, tooth reduction should be performed conservatively in AI patients. A baseline dental radiograph can provide information regarding enamel thickness and pulp. This information is helpful to avoid any mechanical pulp exposure during tooth reduction. Some reports suggested that placing separators interproximally before tooth reduction will help to preserve tooth structure (Sapir and Shapira, 2007; Ng and Messer, 2009). In conclusion, early diagnosis and timely interventions prevent AI patients from early loss of teeth that will inevitably complicate treatment needs.

It was also interesting to note that twenty permanent mandibular incisors had no restorations. One explanation may be that those incisors were partially erupted or symptom free.

In the Lindunger and Smedberg study, hypomineralized AI patients had a higher plaque index, bleeding index and pocket depth when compared to hypoplastic AI patients (Lindunger and Smedberg, 2005). In this study, this statement could not be tested due to its small sample size. It is interesting that subject 5, affected with hypocalcified AI, had a high score in both plaque index (PI=3) and in gingival index (GI= 2.9) compared with other subjects suffering from different types of AI. This particular subject also had two

stainless steel crowns with deep pocket depth (value ≥ 4). This finding may indicate that this subject did not keep up optimal oral hygiene.

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Study limitations

There were limitations to the current study and its conclusions should be taken with caution. First, due to the specific study objective, and the particular stage of treatment being assessed, the number of subjects recruited for this study was very small. In addition, there was no comparable control group available. Second, these restorations were evaluated at one time point only. No baseline data was available, therefore was impossible to know how changes took place over time. Third, these fifty-nine restorations were from only seven subjects. Therefore, it is not meaningful to conduct statistical analyses on the clinical and periodontal outcomes obtained from four different types of restoration placed on teeth affected by 3 different types of AI. With this small of a sample, the authors could not investigate the impact of the severity of AI phenotype on the different types of restoration. Potential limitations of our survey may include that subjects' answers to the survey questions which are applicable before and after treatment, were given at the same time. Subjects may have forgotten what they really felt before the treatment.

Conclusions

Based on the study results, the following conclusions can be made:

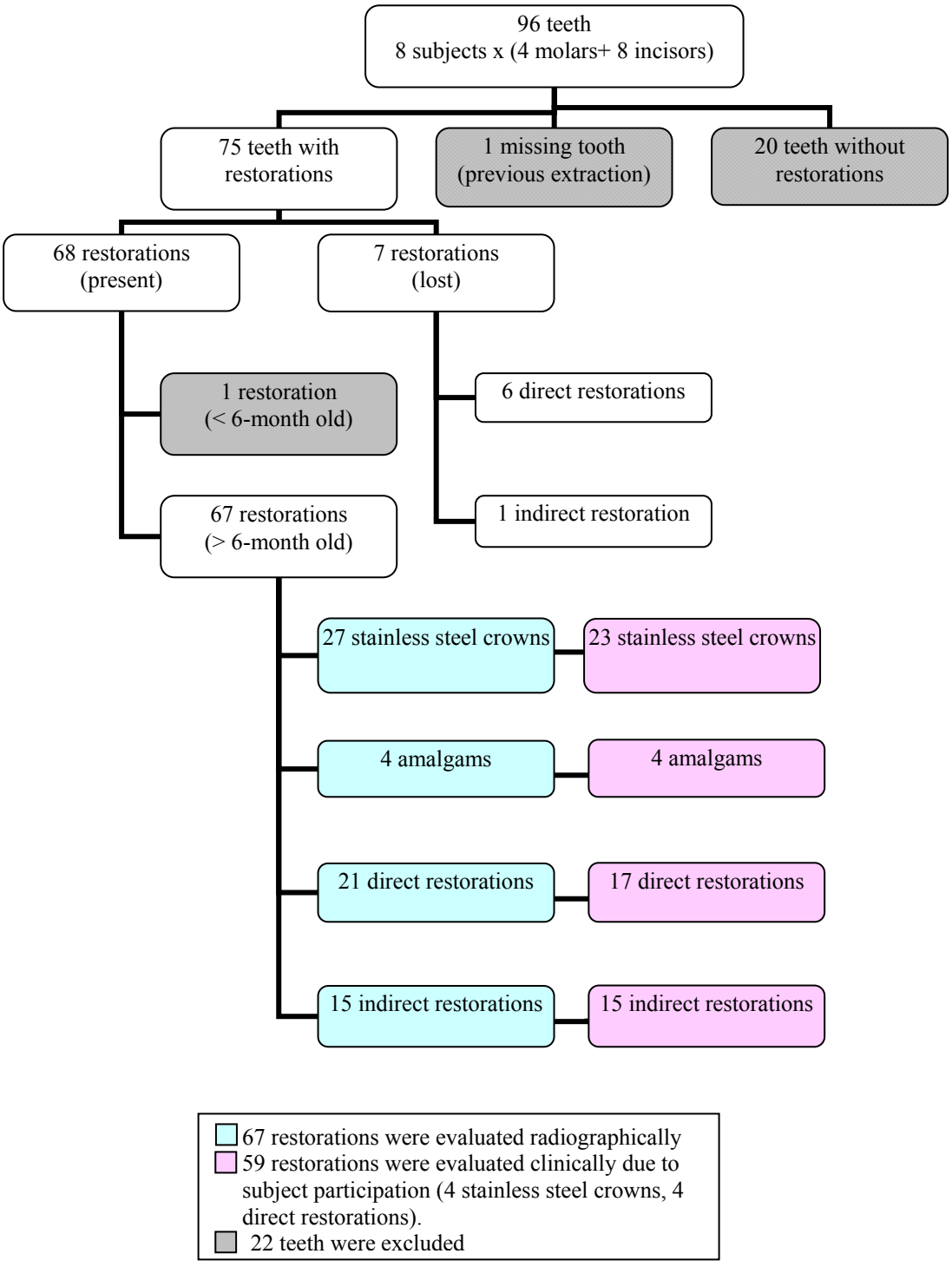
1. During the mixed dentition stage, teeth with AI can be restored using conventional treatment modalities. Direct restorations, such as composite resin strip crowns and fewer than 4-surface composite resin restoration, have a high percentage of unacceptable and failed restorations (12/23). They should only be considered as "interim restorations" and multiple repairs and replacements have to be expected. Periodic maintenance will be necessary to keep such interim direct restorations intact and functional.
2. Gingival inflammation and plaque accumulation were observed following restorative treatment of patients with AI.
3. Patients with AI were satisfied with their appearance and expressed a decrease in sensitivity with eating and brushing after restorative treatment.

Future Research Based on This Study

Further research into several aspects is required to strengthen the outcome of this study. Comparisons of the oral health status before and after restorative treatment of patients with different variants of AI will enable determination of effectiveness of specific restorations for each type of AI. Furthermore, studies of qualitative and /or quantitative change of the saliva would provide important insight into the cause of periodontal problems in AI patients. Also, researchers may evaluate well-documented restorations at fixed time points and conduct a survival analysis in order to gain information on durability and sustainability of restorations.

List of Figure

Figure 1 The Distribution of Teeth



List of Tables

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Subject	AI type[1]	Sex	Age	Type of restoration				Missing[3]	No restoration[4]
				Stainless steel crown	Amalgam	Direct restoration[2]	Indirect restoration		
1	1	F	13y7m	4	0	8	0	0	0
2	2	F	12y5m	4	0	4	0	0	4
3	1	F	15y9m	4	0	8	0	0	0
4	1	M	15y7m	4	0	2	4	0	2
5	2	F	9y4m	4	0	2	0	0	6
6	3	M	13y2m	4	0	0	0	0	8
7	3	F	14y	1	3	0	8	0	0
8	1	F	15y	2	1	4	4	1	0
Total				27	4	28	16	1	20

[1] AI type: 1= hypoplastic; 2= hypocalcified; 3=hypocalcified- hypomaturation
[2] The age of one direct restoration was less than 6-month old thus was excluded.
[3] One missing tooth was excluded. (extracted prior to first clinic visit)
[4] Twenty teeth without restorations were excluded.

Table 2: Summary of Restorations (N=67) and Tooth Type Evaluated with Age of Placement Calculated [1]

Type of restoration	Tooth type	AI1[2]	AI2[3]	AI3[4]	Total	Restoration age (months)				
						mean	Std. deviation	median	minimum	maximum
Stainless steel crown	Molar	14	8	5	27	49.33	35.60	27.00	9	100
Amalgam	Molar	1	0	3	4	13.00	3.46	11.00	11	17
Direct restoration	Incisor	17	4	0	21	45.29	28.32	41.00	9	81
Indirect restoration	Incisor	7	0	8	15	14.73	14.68	8.00	6	43

[1] A total of 67 restorations were present at the date of evaluation. Not included were 7 lost restorations and one direct restoration, which was less than 6-month old.
[2] AI1= hypoplastic AI
[3] AI2= hypocalcified AI
[4] AI3=hypocalcified- hypomaturation AI

Table 3: Clinical Evaluation of Restorations (N=59)[1, 2]

Type of restoration (Number)	Surface		Color		Form		Margin		Fractures		Caries		Wear		Total score	
	A	U	A	U	A	U	A	U	A	U	A	U	A	U	A	U
Stainless steel crown[3] (23)	n/a		n/a		n/a		23	0	n/a		23	0	22	1	22	1
Amalgam[3] (4)	3	1	n/a		4	0	4	0	4	0	4	0	n/a		3	1
Direct restoration[3] (17)	15	2	17	0	15	2	13	4	17	0	16	1	n/a		11	6
Indirect restoration[3] (15)	15	0	15	0	15	0	13	2	n/a		15	0	15	0	13	2
Total (59)	33	3	32	0	34	2	53	6	21	0	58	1	37	1	49	10

[1] Based on the modified U.S. Public Health Service criteria. Restorations were rated as "A" if they received every score in the acceptable range. Restorations were rated as "U" if they had a score in any of unacceptable range.

[2] Fifty-nine restorations were evaluated. One subject (4 stainless steel crowns and 4 direct restorations) did not participate in clinical evaluation.

[3] n/a= not applicable

Table 4: Summary of Clinical Restorations Failures (N=66)[1]

Type of restoration	Number of teeth	Lost Restoration[2]	Unacceptable Restoration[3]	Total failure
Stainless steel crown	23	0	1	1
Amalgam	4	0	1	1
Direct restoration	23	6	6	12
Indirect restoration	16	1	2	3
Total	66	7	10	17

[1] Sixty-six teeth were evaluated including: 59 teeth with restorations and 7 teeth that lost restorations.
[2] Lost restorations were based on initial chart review.
[3] Unacceptable restorations were based on clinical evaluation of restorations

Table 5: Frequency of Retreatment (N=11)

Type of restoration	Number	Type of repair	Time to first repair (in months)				
			Mean	Std. deviation	median	minimum	maximum
Stainless steel crown	3	Replacement	24.14	11.51	27.83	11.24	33.35
Direct restoration	7	add composite	22.94	27.35	9.82	2.14	75.73
Indirect restoration	1	Recement	0.5	-	0.5	0.5	0.5

Table 6: Assessment of Periodontal Conditions Associated with Various Types of Restoration (N=59) [1].

Type of restoration (Number of teeth)	Gingival index [2]	Value≥3	Plaque index[3]	Value≥4	Pocket depth	Value≥4	Bleeding on probing
	mean (SD)	n/total (%)	mean (SD)	n/total (%)	mean (SD)	n/total (%)	n/total (%)
Stainless steel crown (23)	2.30 (0.69)	4/23 (17.4%)	2.00 (0.92)	6/23 (26%)	2.02 (0.67)	3/23 (13.0%)	20/23 (87.0%)
Amalgam (4)	1.75 (0.29)	0/4	1.63 (0.63)	0/4	2.08 (0.24)	0/4	1/4 (25%)
Direct restoration (17)	2.29 (0.77)	7/17 (41.2%)	1.47 (0.37)	0/17	1.44 (0.26)	0/17	12/17 (70.6%)
Indirect restoration (15)	1.63 (0.58)	2/15 (13.3%)	1.10 (0.21)	0/15	2.10 (0.20)	0/15	14/15 (93.3%)

[1] Fifty-nine restorations were evaluated. Four stainless steel crowns and 4 direct restorations were not evaluated due to subject participation.
[2] Score ranged from "0"= no inflammation to "3"= severe inflammation.
[3] Score ranged from "0"= no plaque/ debris to "5"= plaque covering two thirds or more of the clinical crown.

Table 7: Radiographic Evaluation of Restorations (N=67)

Type of restoration (Number)	PDL widening	Pulp canal obliteration	Overhang margin	Open margin	Small crown	Fracture restoration	Margin discrepancy ≤2mm	Furca /apical radiolucency
Stainless steel crown (27)	4	3	1	2	6	0	9	0
Amalgam (4)	0	1	0	0	0	0	0	0
Direct restoration (21)	3	1	4	3	1	0	0	0
Indirect restoration (15)	1	0	1	2	0	0	0	0
Total	8	5	6	7	7	0	9	0

Table 8: Outcome of Survey (N=8)[1]

		Mean[2]	Paired t-test p-value
Do you smile for pictures?	Before treatment	2.43	.140
	After treatment	1.71	
Do you like the way your teeth look?	Before treatment	4.43	.002[3]
	After treatment	1.57	
Are you able to eat regular food?	Before treatment	3.71	.093
	After treatment	2.43	
How sensitive are your teeth? When tooth brushing	Before treatment	3.00	.025[3]
	After treatment	1.67	
How sensitive are your teeth? When eating	Before treatment	3.29	.010[3]
	After treatment	1.71	

[1] One subject did not answer the after treatment questions due to treatment in progress.
[2] On a scale of five, subjects indicated their answer to each question from 1 (best) to 5 (worst) subjectively.
[3] Denotes statistical significance ($p<0.05$)

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Appendix A

Institutional Review Board Approval Letter

UNIVERSITY OF MICHIGAN
eResearch.umich.edu
Health Sciences and Behavioral Sciences Institutional Review Board • 540 East Liberty Street, Suite 202, Ann Arbor, MI 48104-2210 • phone (734) 936-0933 • fax (734) 998-9171 • irbhsbs@umich.edu

To: Chiung-Fen Chen

From:
Richard Redman

Cc:
Mathilde Peters
Chiung-Fen Chen
Eduardo Bresciani
(Ninna) Maria Regina Estrella
Jan Hu

Subject: Initial Study Approval for [HUM00027771]

SUBMISSION INFORMATION:
Study Title: Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage
Full Study Title (if applicable):
Study eResearch ID: HUM00027771
Date of this Notification from IRB: 9/8/2009
Initial IRB Approval Date: 7/23/2009
Current IRB Approval Period: 7/23/2009 - 7/22/2010
Expiration Date: Approval for this expires at **11:59 p.m. on 7/22/2010**
UM Federalwide Assurance (FWA): FWA00004969 expiring on 11/17/2011
OHRP IRB Registration Number(s): IRB00000245

NOTICE OF IRB APPROVAL AND CONDITIONS:
The IRB HSBS has reviewed and approved the study referenced above. The IRB determined that the proposed research conforms with applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS). You must conduct this study in accordance with the description and information provided in the approved application and associated documents.

APPROVAL PERIOD AND EXPIRATION:
The approval period for this study is listed above. Please note the expiration date. If the approval lapses, you may not conduct work on this study until appropriate approval has been re-established, except as necessary to eliminate apparent immediate hazards to research subjects. Should the latter occur, you must notify the IRB Office as soon as possible.

IMPORTANT REMINDERS AND ADDITIONAL INFORMATION FOR INVESTIGATORS

APPROVED STUDY DOCUMENTS:
You must use any date-stamped versions of recruitment materials and informed consent documents available in the eResearch workspace (referenced above). Date-stamped materials are available in the "Currently Approved Documents" section on the "Documents" tab.

RENEWAL/TERMINATION:
At least two months prior to the expiration date, you should submit a continuing review application either to renew

or terminate the study. Failure to allow sufficient time for IRB review may result in a lapse of approval that may also affect any funding associated with the study.

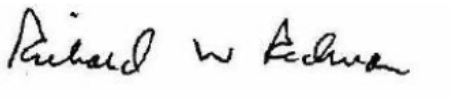
AMENDMENTS:
All proposed changes to the study (e.g., personnel, procedures, or documents), must be approved in advance by the IRB through the amendment process, except as necessary to eliminate apparent immediate hazards to research subjects. Should the latter occur, you must notify the IRB Office as soon as possible.

AEs/ORIOs:
You must inform the IRB of all unanticipated events, adverse events (AEs), and other reportable information and occurrences (ORIOs). These include but are not limited to events and/or information that may have physical, psychological, social, legal, or economic impact on the research subjects or others.

Investigators and research staff are responsible for reporting information concerning the approved research to the IRB in a timely fashion, understanding and adhering to the reporting guidance (http://www.med.umich.edu/irbmed/ae_orio/index.htm), and not implementing any changes to the research without IRB approval of the change via an amendment submission. When changes are necessary to eliminate apparent immediate hazards to the subject, implement the change and report via an ORIO and/or amendment submission within 7 days after the action is taken. This includes all information with the potential to impact the risk or benefit assessments of the research.

SUBMITTING VIA eRESEARCH:
You can access the online forms for continuing review, amendments, and AEs/ORIOs in the eResearch workspace for this approved study (referenced above).

MORE INFORMATION:
You can find additional information about UM's Human Research Protection Program (HRPP) in the Operations Manual and other documents available at: www.research.umich.edu/hrpp.



Richard Redman
Chair, IRB HSBS

UNIVERSITY OF MICHIGAN
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Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Chiung-Fen Chen

From:
Michael Geisser
John Weg

Cc:
Mathilde Peters
Chiung-Fen Chen
Eduardo Bresciani
(Ninna) Maria Regina Estrella
Jan Ching Chun Hu
Angela Meneghini

Subject: Amendment [Ame00017904] Approved for [HUM00027771]

SUBMISSION INFORMATION:
Study Title: Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage
Full Study Title (if applicable):
Study eResearch ID: HUM00027771
Amendment eResearch ID: Ame00017904
Amendment Title: HUM00027771_Amendment - Sun May 9 19:33:39 EDT 2010
Date of this Notification from IRB: 8/19/2010
Date of Approval for this Amendment: 8/12/2010
Current IRB Approval Period: 7/21/2010 - 7/20/2011
Expiration Date: Approval for this expires at **11:59 p.m. on 7/20/2011**
UM Federalwide Assurance (FWA): FWA00004969 expiring on 11/17/2011
OHRP IRB Registration Number(s): IRB00001999

Approved Risk Level(s) as of this Amendment:

Name	Risk Level
HUM00027771	No more than minimal risk

NOTICE OF IRB APPROVAL AND CONDITIONS:
The IRBMED has reviewed and approved the amendment to the study referenced above. The IRB determined that the proposed research continues to conform with applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS). You must conduct this study in accordance with the description and information provided in the approved application and associated documents, as amended.

APPROVAL PERIOD AND EXPIRATION: The approval period for this study is listed above. Please note the expiration date is not changed by the approval of this amendment. If the approval lapses, you may not conduct work on this study until appropriate approval has been re-established, except as necessary to eliminate apparent immediate hazards to research subjects. Should the latter occur, you must notify the IRB Office as soon as possible.

IMPORTANT REMINDERS AND ADDITIONAL INFORMATION FOR INVESTIGATORS

APPROVED STUDY DOCUMENTS:
You must use any date-stamped versions of recruitment materials and informed consent documents available in the eResearch workspace (referenced above). Date-stamped materials are available in the "Currently Approved Documents" section on the "Documents" tab.

RENEWAL/TERMINATION:
At least two months prior to the expiration date, you should submit a continuing review application either to renew or terminate the study. Failure to allow sufficient time for IRB review may result in a lapse of approval that may also affect any funding associated with the study.

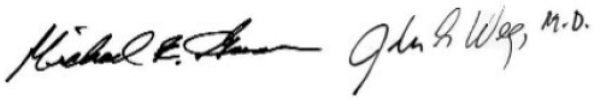
FUTURE AMENDMENTS:
All proposed changes to the study (e.g., personnel, procedures, or documents), must be approved in advance by the IRB through the amendment process, except as necessary to eliminate apparent immediate hazards to research subjects. Should the latter occur, you must notify the IRB Office as soon as possible.

AEs/ORIOs:
You must inform the IRB of all unanticipated events, adverse events (AEs), and other reportable information and occurrences (ORIOs). These include but are not limited to events and/or information that may have physical, psychological, social, legal, or economic impact on the research subjects or others.

Investigators and research staff are responsible for reporting information concerning the approved research to the IRB in a timely fashion, understanding and adhering to the reporting guidance (http://www.med.umich.edu/irbmed/ae_orio/index.htm), and not implementing any changes to the research without IRB approval of the change via an amendment submission. When changes are necessary to eliminate apparent immediate hazards to the subject, implement the change and report via an ORIO and/or amendment submission within 7 days after the action is taken. This includes all information with the potential to impact the risk or benefit assessments of the research.

SUBMITTING VIA eRESEARCH:
You can access the online forms for continuing review, amendments, and AEs/ORIOs in the eResearch workspace for this approved study, referenced above.

MORE INFORMATION:
You can find additional information about UM's Human Research Protection Program (HRPP) in the Operations Manual and other documents available at: www.research.umich.edu/hrpp.



Michael Geisser
Co-chair, IRBMED

John Weg
Co-chair, IRBMED

Appendix B

Script for Calling Parent/ Guardian

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage
Chiung-Fen Chen, DDS

Graduate Pediatric Dentistry Clinic, University of Michigan

SCRIPT FOR CALLING PARENT/GUARDIAN

Hello! May I please speak to the parent or guardian of _____ (*child's name*)?

Hi! This is _____ (*Dr. Estrella / Dr. Chen)* calling from the University of Michigan Pediatric Dentistry Clinic. I understand that _____ (*child's name*) has an upcoming check-up and cleaning at our clinic. Also, I understand that _____ (*child's name*) has AI.

I am doing a study about dental treatment of children with AI. I would like to know if you are interested in learning more about this study.

(if parent responds yes, continue…)

First, can I ask you a few questions?

1. How old is your child?
2. Has he / she completed dental treatment at our clinic?
3. Does he/she having braces? (if the answer is yes→ excluded)

(if the answer to #3 is no, continue…)

I would like to invite your child to participate in our study at his/her next dental check-up. After their normal cleaning and check-up exam, your child will have a gum exam, his/her fillings and caps checked, pictures (photos) of their teeth taken and some x-rays taken for the study. I will also ask your child to answer 10 questions about how they feel about their teeth and filling. All these procedures might take approximately an hour. Are you interested in learning more about this study?

(if parent answers yes)

Great! Please call us and schedule a recall appointment and inform the receptionist that you are interested in the AI study. When you arrive, inform our front desk that you are here for the: "AI Study."

Date of the phone call

Study No.: HUM00027771 Consent Approved On: 7/23/2009 Project Approval Expires On: 7/20/2011
IRB: IRB00000245

Appendix C
Parent Consent Form

University of Michigan
Parental Consent for participation in the study on
"Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage"

Names of Researchers:
Chiung-Fen Chen, DDS, Maria Regina (Ninna) Estrella, DDS, MS, Jan CC Hu, BDS, Ph.D
Eduardo Bresciani, BDS, MS, Ph.D, Mathilde C Peters, DMD, PhD

The purpose of this study is to evaluate the dental treatment done to fix your child's teeth affected with Amelogenesis Imperfecta (AI). We would like to know how his/her fillings and caps are doing and how your child feels about his/her teeth. If you agree to let your child participate in the study, you will need to sign this consent form. Your child will also be asked if they want to participate in our study.

Today your child will have a cleaning, exams, and two to four x-rays as part of his/her normal check-up. After this, we will conduct the study. The study will consist of a review of your child's dental record, 5 to 13 pictures/photographs of your child's teeth, examination of your child's gums, fillings and caps, and an extra 10 x-rays. If your child already had x-rays taken in the normal check-up, we will not take these x-rays again. We will also ask your child 10 questions about how he/she feels about his/her teeth. These procedures will take approximately one hour.

Your child's risks may include discomfort and/or sensitivity during our exam. He/ She can ask for breaks at any point in the exam to reduce the discomfort. The total x-ray exposure today will be less than playing outside under the sun for a whole summer. Your child may choose to stop/quit at any time during any part of study. If later you believe that your child feels any discomfort, please contact us. We do not anticipate any lasting discomfort or sensitivity but if your child experiences any lasting discomfort or sensitivity please contact us so we can assist you in making your child comfortable.

Your child will get a $20 Meijer gift certificate at the end of today's visit. If your child decides to quit before all exams are over, he/she will still get $20 gift certificate.

We hope the results of this study will help us understand how the fillings and caps in your child's mouth are doing and how patients affected by Amelogensis Imperfecta feel about their teeth. This may help us to provide better care for children with Amelogensis Imperfecta in the future.

There will be no additional cost to particpate in this study. You will not be charged for the extra photos, x-rays and examination and we will give you a parking voucher for today's visit. However, you are responsible for the fees associated with the normal check-up during your child's recall examination.

Taking part in this study is voluntary for your child. You do not have to let your child participate. Even after you consent, you have a right to withdraw your child from this study at any time. If your child leaves the study before it is finished, there will be no penalty and it will not affect his/her future treatment at our clinic. This information we collect will be destroyed if you or your child decides to quit the study after we have started.

The information might be kept for up to five years for future studies. We plan to report the results of this study, but it will not include any information that would identify your child. We will enter study data on a computer that is password-protected.

Study No.: HUM00027771 **Consent Approved On: / /** **Project Approval Expires On: 7/20/2011**
IRB: IRB00000245

You may contact Dr. Chiung-Fen Chen or Dr. Ninna Estrella, at (734) 764-1523, to ask any questions about the research, or any issue you may feel is related to the study. Additionally, you can contact the University of Michigan Medical School Institutional Review Board (IRBMED), 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800. Telephone: (734) 763-1234; Fax: (734) 763-1234; Email: irbmed@umich.edu. if you have questions concerning the rights of research subjects.

By signing this form, you are consenting to allow your child to participate in the study. You also agree that we have answered your questions about the study and you understand what your child is being asked to do. You may contact us if you think of a question later. We will give you a copy of this form and will keep one for our study records.

I give my permission for my child to participate in this study.

_____ _____

Name (Print)/Date Signature

I give my permission for researchers to keep data for five years.

_____ _____

Name (Print)/Date Signature

Child's name (Print): _____ Relationship _____

_____ _____

Witness (Print) Witness signature

Appendix D
Subject Assent Form

University of Michigan

Assent of Child (age 8-13)

" Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage "

Names of Researchers:

Chiung-Fen Chen, DDS, Maria Regina (Ninna) Estrella, DDS, MS, Jan CC Hu, BDS, Ph.D
Eduardo Bresciani, BDS, MS, Ph.D, Mathilde C Peters, DMD, PhD

We are working on a study about how your fillings and caps are doing and how you feel about your teeth.

Today you will have a cleaning, exam, and possible x-rays as part of your normal check-up, If you choose to be in our study, we will check your teeth, gums, fillings and caps again. We will also take x-rays and pictures (photos) of your teeth. The total x-ray exposure today will be less than playing outside under the sun for a whole summer. When we are all done we will ask you 10 questions about how you feel about your teeth. The study will take about one hour but you may ask for breaks at any time. When we measure your gums and take pictures and x-rays you might get tired or feel some discomfort, it will help if you take breaks. You can ask for breaks whenever you want during any part of study. It is okay for you to stop or quit the study at any time during any part of the study. Your parents have already said it would be okay for you to be part of the study but only if you choose to participate.

You will get a $20 prize from Meijer at the end of today's visit. Even if you quit the study, you will still get a prize.

Your information might be kept for five years for future studies. We plan to report the results of this study, but will not include your name.

Do you want to be part of our study?

I agree to be part of this study.

_____ _____

Name (Print)/Date Signature

I agree to have my information kept for five years for further studies.

_____ _____

Name (Print)/Date Signature

_____ _____

Witness (Print)/Date Witness signature

Study No.: HUM00027771 **Assent Approved On: //** **Project Approval Expires On: 7/20/2011**
IRB: IRB00000245

University of Michigan
Assent of Child (age 14-17)
" Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage "

Names of Researchers:
Chiung-Fen Chen, DDS, Maria Regina (Ninna) Estrella, DDS, MS, Jan CC Hu, BDS, Ph.D
Eduardo Bresciani, BDS, MS, Ph.D, Mathilde C Peters, DMD, PhD

We are asking you to be part of a study that looks at the fillings and caps that were put on your teeth. We want to know how your fillings and caps are doing and how you feel about your teeth.

Today you will have a cleaning, exam, and possible x-rays as part of your normal check-up. If you agree to participate in this study, we will collect some more information about your teeth. We will look at your dental records, take 5 to 13 pictures (photos) of your teeth, check your gums, fillings and caps, and take an extra 10 x-rays. If you already had x-rays done at the normal check-up, we will not take these x-rays again. At the end, we will ask you to answer 10 questions about how you feel about your teeth. The study will take about one hour.

The risks involved in participating in our study include: slight discomfort and/or sensitivity during our exam, which can be reduced with breaks. The total x-ray exposure today will be less than playing outside under the sun for a whole summer. If you feel uncomfortable, you can ask for breaks during any part of study and you may choose to stop or quit at any time.

You will get a $20 Meijer gift certificate at the end of today's visit. Even if you quit the study, you will still get a $20 Meijer gift certificate.

We hope the results of this study will help us understand how the fillings and caps are doing and how you feel about your teeth. This may help us take better care of other children with teeth like yours.

Taking part in this study is your choice. You do not have to participate if you do not want to, even if your parents say you can. You may stop at any time. It is okay if you quit before the study is finished and the information we collect will be destroyed.

The information might be kept up to five years for future studies. We plan to report the results of this study, but your name will not be included. We will enter the study data on a computer that is safe.

You may contact Dr. Chiung-Fen Chen or Dr. Ninna Estrella, at (734) 764-1523, to ask any questions about the study, including your rights and concerns. If you like, you can contact the University of Michigan Medical School Institutional Review Board to ask them about your rights as a study participant. They can be reached at University of Michigan Medical School Institutional Review Board (IRBMED), 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800. Telephone: (734) 763-1234; Fax: (734) 763-1234; Email: irbmed@umich.edu.

Study No.:HUM00027771 **Assent Approved On: //** **Project Approval Expires On: 7/20/2011**
IRB: IRB00000245

By signing this form, you are saying yes to participate in the study. You also agree that we have answered your questions about the study and you understand what you are being asked to do. You may contact us if you think of a question later. We will give you a copy of this form and will keep a copy as our records.

I agree to participate in this study

Name (Print)/Date	Signature

I agree to have my information kept for five years for further studies

Name (Print)/Date	Signature
Witness (Print)/Date	Witness signature

Appendix E
Subject Consent

University of Michigan
Consent for participation in the study on
" Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage "

Names of Researchers:
Chiung-Fen Chen, DDS, Maria Regina (Ninna) Estrella, DDS, MS, Jan CC Hu, BDS, Ph.D
Eduardo Bresciani, BDS, MS, Ph.D, Mathilde C Peters, DMD, PhD

We are asking you to participate in our study that evaluates your fillings and caps. We would like to know how your fillings and caps are doing and how you feel about your teeth.

Today, you will have a cleaning, exam, and two to four x-rays as part of your normal check up. If you agree to participate in this study we will collect additional information about your teeth. We will look at your dental records, take 5 to 13 pictures (photos) of your teeth, check your gums, fillings and caps, and take an extra 10 x-rays. If you already had x-rays done at the normal check-up, we will not take these x-rays again. At the end, we will ask you to answer 10 questions about how you feel about your teeth. The study exam will take about one hour.

The risks involved in participating in our study include: slight discomfort and/or sensitivity during our exam which can be reduced with breaks. The total x-ray exposure today will be less than playing outside under the sun for a whole summer. If you feel uncomfortable, you can ask for breaks during any part of study and you may choose to stop at any time.

You will get a $20 Meijer gift certificate at the end of today's visit. Even if you do not complete the study, you will still get a gift certificate.

We hope the results of this study will help us understand how the fillings and caps are doing and how children affected by Amelogenis Imperfecta feel about their teeth. This may help us to provide better care for children with AI in the future..

Taking part in this study is voluntary. You do not have to participate if you do not want to. Even after you consent, you have a right to withdraw from this study at any time. If you leave the study before it is finished, there will be no penalty to you and your future treatment at our clinic. The information we collect will be destroyed if you choose to withdraw.

The information might be kept up to five years for future studies. We plan to report the results of this study, but any information that would identify you will be not included.

You may contact Dr. Chiung-Fen Chen or Dr. Ninna Estrella, at (734) 764-1523, to ask any questions about the research, or any issue you may feel related to the study. Additionally, you can contact the University of Michigan Medical School Institutional Review Board (IRBMED), 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800. Telephone: (734) 763-1234; Fax: (734) 763-1234; Email: irbmed@umich.edu., if you have questions concerning the rights of research subjects.

By signing this form, you are agreeing to participate in the study. You also agree that we have answered your questions about the study. You may contact us if you think of a question later. We will give you a copy of this form and will keep one for our study records.

Study No.: HUM00027771 **Consent Approved On: / /** **Project Approval Expires On: 7/20/2011**
IRB: IRB00000245

I agree to participate in this study.

Name (Print)/Date	Signature

I give my permission for researchers to keep data for five years.

Name (Print)/Date	Signature
Witness (Print) /Date	Witness signature

Appendix F
Chart Review

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage

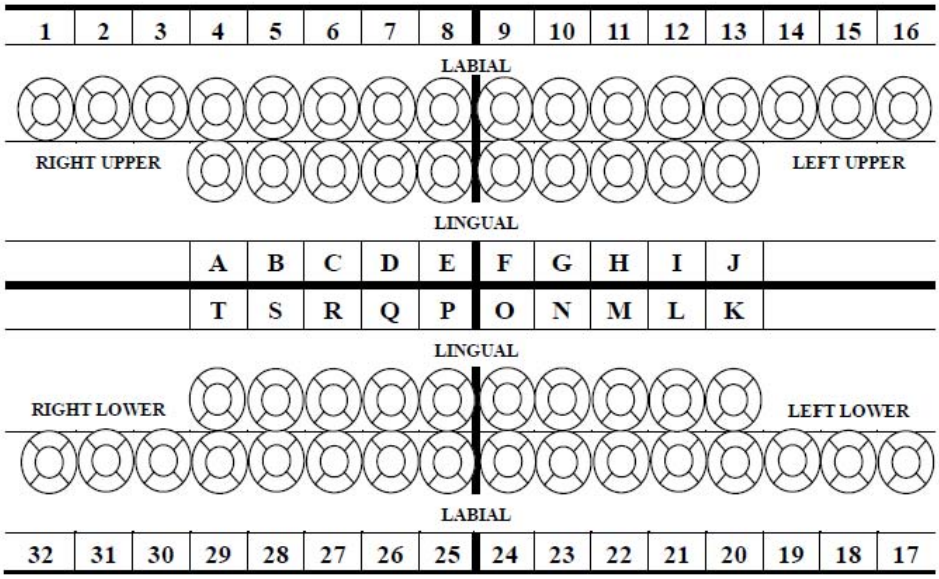
Chiung-Fen Chen, DDS

Pediatric Dentistry Clinic, University of Michigan

Chart Review

Date of appt. _____/_____/_____ **ID No.:_____**

DOB: _____/_____/_____



Date of last exam :_____

Additional note

Periodontal surgery:_____

Orthodontic treatment:_____

Space maintainer:_____

Appendix G

Composite Resin/ Amalgam Restoration Evaluation Guideline
and
Restoration Examination Form

Composite Resin/ Amalgam Restoration Evaluation Guideline

Quality Evaluation Criteria and Abbreviations

Severity	1. Surface	2. Color of match (comp. only)	3. Anatomic form	4. Marginal integrity	5. Fracture restoration	6. Caries at margin
WNL (acceptable)	**1.0** Surface of the restoration is smooth.	**2.0** No color mismatch between restoration and adjacent tooth or teeth.	**3.0** Restoration contour follows the contour of the teeth.	**4.0** No evidence of a crevice along margin.	**5.0** No fracture	**6.0** No caries
Mild/ Moderate (acceptable)	**1.1** Surface of restoration is slightly rough or pitted	**2.1** Slight color mismatch between restoration and adjacent tooth or teeth	**3.1.1** Restoration is slightly over contoured **3.1.2** Restoration is slightly under contoured	**4.1** slight marginal discrepancy. Gap < 0.4 mm	**5.1** Partial restoration fracture	**6.1** White spot lesion
Severe (unacceptable)	**1.2** Surface of restoration is rough, unacceptable plaque retentive surface	**2.2** Shade in gross disharmony with adjacent teeth.	**3.2.1** Restoration is grossly under contoured **3.2.2** Restoration is Grossly Over Contoured	**4.2** Faulty margins	**5.2** Restoration fracture	**6.2** Cavitation

Modified from U.S. Public Health Service criteria
WNL: within normal limit

Direct Composite resin /Amalgam.

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage

Chiung-Fen Chen, DDS

Pediatric Dentistry Clinic, University of Michigan

Restoration Examination

Date_____/_____/_____ **ID No.:**_____

Restoration type: **Amalgam/ comp.**	Surface	Color of match (comp.only)	Anatomic form	Marginal integrity	Fracture restoration	Caries at margin
	1.0	2.0	3.0	4.0	5.0	6.0
	1.1	2.1	3.1.1 3.1.2	4.1	5.1	6.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	5.2	6.2

Restoration type: **Amalgam/ comp.**	Surface	Color of match (comp.only)	Anatomic form	Marginal integrity	Fracture restoration	Caries at margin
	1.0	2.0	3.0	4.0	5.0	6.0
	1.1	2.1	3.1.1 3.1.2	4.1	5.1	6.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	5.2	6.2

Restoration type: **Amalgam/ comp.**	Surface	Color of match (comp.only)	Anatomic form	Marginal integrity	Fracture restoration	Caries at margin
	1.0	2.0	3.0	4.0	5.0	6.0
	1.1	2.1	3.1.1 3.1.2	4.1	5.1	6.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	5.2	6.2

Appendix H

Indirect Restoration Evaluation Guideline
and
Restoration Examination Form

Indirect Restoration Evaluation Guideline

Quality Evaluation Criteria and Abbreviations

Severity	1. Surface	2. Color of match	3. Anatomic form	4. Marginal adaptation	6. Caries at margin	7. Wear
WNL (acceptable)	**1.0** Surface of the restoration is smooth.	**2.0** No color mismatch between restoration and adjacent tooth or teeth.	**3.0** Restoration contour follows the contour of the teeth.	**4.0** No gaps	**6.0** No caries	**7.0** Physiological wear
Mild/ moderate (acceptable)	**1.2** Surface of restoration is slightly rough or pitted	**2.1** Slight color mismatch between restoration and adjacent tooth or teeth	**3.1.1** Restoration is slightly over contoured **3.1.2** Restoration is slightly under contoured	**4.1** Gap < 0.4mm	**6.1** White spot lesion	**7.1** Facet
Severe (unacceptable)	**1.2** Surface of restoration is rough, unacceptable plaque retentive surface	**2.3** Shade in gross disharmony with adjacent teeth.	**3.2.1** Restoration is grossly under contoured **3.2.2** Restoration is grossly over contoured	**4.2** Gap > 0.4mm	**6.2** Cavitation	**7.2** Perforated

Modified from U.S. Public Health Service criteria

WNL: within normal limit

Indirect restorations

Restoration type:	Surface	Color of match	Anatomic form	Marginal adaptation	Caries at margin	wear
Indirect	1.0	2.0	3.0	4.0	6.0	7.0
restorations	1.1	2.1	3.1.1 3.1.2	4.1	6.1	7.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	6.2	7.2

Restoration type:	Surface	Color of match	Anatomic form	Marginal adaptation	Caries at margin	Wear
Indirect	1.0	2.0	3.0	4.0	6.0	7.0
restorations	1.1	2.1	3.1.1 3.1.2	4.1	6.1	7.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	6.2	7.2

Restoration type:	Surface	Color of match	Anatomic form	Marginal adaptation	Caries at margin	wear
Indirect	1.0	2.0	3.0	4.0	6.0	7.0
restorations	1.1	2.1	3.1.1 3.1.2	4.1	6.1	7.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	6.2	7.2

Restoration type:	Surface	Color of match	Anatomic form	Marginal adaptation	Caries at margin	wear
Indirect	1.0	2.0	3.0	4.0	6.0	7.0
restorations	1.1	2.1	3.1.1 3.1.2	4.1	6.1	7.1
Tooth No.:	1.2	2.2	3.2.1 3.2.2	4.2	6.2	7.2

Appendix I

Stainless Steel Crown Restoration Guideline
and
Restoration Examination Form

Stainless Steel Crown Restoration Evaluation Guideline

Quality Evaluation Criteria and Abbreviations

Severity	4. Marginal adaptation	6. Caries at margin	7. Wear
WNL (acceptable)	**4.0** No gaps	**6.0** No caries	**7.0** Physiological wear
Mild/ Moderate (acceptable)	**4.1** Gap < 0.4 mm	**6.1** White spot lesion	**7.1** Facet
Severe (unacceptable)	**4.2** Gap > 0.4mm	**6.2** Cavitation	**7.2** Perforated:

Modified from U.S. Public Health Service criteria

WNL: within normal limit

SSC

Restoration type:	Marginal adaptation	Caries at margin	wear
SSC	4.0	6.0	7.0
	4.1	6.1	7.1
Tooth No.:	4.2	6.2	7.2

Restoration type:	Marginal adaptation	Caries at margin	wear
SSC	4.0	6.0	7.0
	4.1	6.1	7.1
Tooth No.:	4.2	6.2	7.2

Restoration type:	Marginal adaptation	Caries at margin	wear
SSC	4.0	6.0	7.0
	4.1	6.1	7.1
Tooth No.:	4.2	6.2	7.2

Restoration type:	Marginal adaptation	Caries at margin	wear
SSC	4.0	6.0	7.0
	4.1	6.1	7.1
Tooth No.:	4.2	6.2	7.2

Restoration type:	Marginal adaptation	Caries at margin	wear
SSC	4.0	6.0	7.0
	4.1	6.1	7.1
Tooth No.:	4.2	6.2	7.2

Appendix J
Modified Gingival Index

Modified Gingival Index

Appearance	Inflammation	Points
Normal	none	0
Slight change in color and mild edema with slight change in texture, roll border	mild	1
Redness, hypertrophy, edema and glazing	moderate	2
Marked redness, hypertrophy, edema, ulceration, purple	severe	3

Gingival Index for a specific tooth = Average of points of 2 surfaces
Gingival Index for patient = Average of Gingival Indices of 12 teeth

Appendix K
Modified Plaque Index

Modified Plaque Index

Turesky et al. Modified Quigley-Hein Plaque Index (TQHPI).

- buccal and lingual aspects on all teeth were scored (i.e., for 28 teeth there was a total of 56 sites). Scoring was as follows:

- **0** = no plaque/debris
- **1** = separate flecks of plaque at the cervical margin of the tooth
- **2** = a thin continuous band of plaque (up to 1 mm) at the cervical margin of the tooth
- **3** = a band of plaque wider than 1 mm but covering less than one third of the crown of the tooth
- **4** = plaque covering at least one third but less than two thirds of the crown of the tooth
- **5** = plaque covering two thirds or more of the crown of the tooth

Appendix L
Periodontal Examination Form

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage

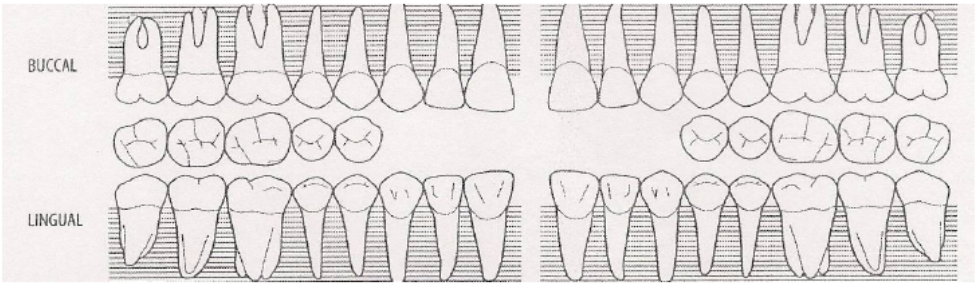
Chiung-Fen Chen, DDS

Pediatric Dentistry Clinic, University of Michigan

Periodontal Exam Form

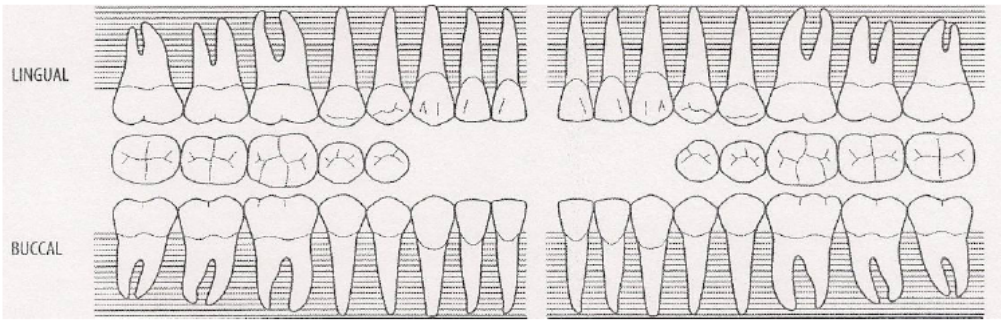
Date of appt. _____/_____/_____ **ID No.:_____**

GI												
PI												
BOP												
PD												
		3		7	8		9	10		14		



		3		7	8		9	10		14		
PD												
BOP												
PI												
GI												

GI												
PI												
BOP												
PD												
		30		26	25		24	23		19		



		30		26	25		24	23		19		
PD												
BOP												
PI												
GI												

Appendix M
Radiographic Examination Form

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage

Chiung-Fen Chen, DDS

Pediatric Dentistry Clinic, University of Michigan

Radiographic Examination

Date of appt. _____/_____/_____ **ID No.:_____**

(Encircle teeth that show abnormalities or the following findings):

Restorative Margin is ≤ 2mm to the Alveolar Crest:

3	7	8	9	10	14
30	26	25	24	23	19

Description:_____

Pathology:

Furcation Radiolucency

3	7	8	9	10	14
30	26	25	24	23	19

Description:_____

Apical Radiolucency

3	7	8	9	10	14
30	26	25	24	23	19

Description:_____

PDL Widening

3	7	8	9	10	14
30	26	25	24	23	19

Description:_____

Additional pathology (i.e. fractures, caries, internal/ external resorption, PCO)

3	7	8	9	10	14
30	26	25	24	23	19

Description:_____

Appendix N
Subject Reported Treatment Outcome

Outcome Assessment of Patients with Amelogenesis Imperfecta who Received Treatment During the Mixed Dentition Stage

Chiung-Fen Chen, DDS

Pediatric Dentistry Clinic, University of Michigan

Subject Reported Treatment Outcome

Date_____/_____/_____ **ID No.:_____**

1 2 3 4 5

1. **Do you smile for pictures?**

a. **before treatment:**

□1 □2 □3 □4 □5

always most of the times sometimes usually not never

b. **after treatment:**

□1 □2 □3 □4 □5

always most of the times sometimes usually not never

2. **Do you like the way your teeth look?**

a. **before treatment:**

□1 □2 □3 □4 □5

definitely yes do not care may be not at all

b. **after treatment:**

□1 □2 □3 □4 □5

definitely yes do not care may be not at all

3. **Are you able to eat regular food? (e.g. meat, ice cream, juice, corn on the cob)**

a. **before treatment:**

□1 □2 □3 □4 □5

very easily easily no problem a little bit difficult very difficult

b. after treatment:

□1	□2	□3	□4	□5
very easily	easily	no problem	a little bit difficult	very difficult

4. How sensitive are your teeth?

During toothbrushing

a. before treatment:

□1	□2	□3	□4	□5
no sensitivity	a little bit sensitive	sensitive	painful	very painful

b. after treatment:

□1	□2	□3	□4	□5
no sensitivity	a little bit sensitive	sensitive	painful	very painful

When eating

a. before treatment:

□1	□2	□3	□4	□5
no sensitivity	a little bit sensitive	sensitive	painful	very painful

b. after treatment:

□1	□2	□3	□4	□5
no sensitivity	a little bit sensitive	sensitive	painful	very painful

1 2 3 4 5

Modified from Wong-Baker face pain-rating scale

Appendix O

Sample Intraoral Photographs and Radiographs