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Article:

Kafourou, V, Tong, HJ, Day, P et al. (2017) Outcomes and prognostic factors that influence the success of tooth autotransplantation in children and adolescents. *Dental Traumatology*, 33 (5). pp. 393-399. ISSN: 1600-4469

<https://doi.org/10.1111/edt.12353>

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Article type : Original Article

**Outcomes and prognostic factors that influence the success of tooth autotransplantation
in children and adolescents**

Title page

Full title of manuscript:

Outcomes and prognostic factors that influence the success of tooth autotransplantation in Children and Adolescents

Running title: Outcomes of autotransplants in children

Keywords: Autotransplantation, donor tooth, periodontal healing, pulp healing, root development

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/edt.12353

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Conflict of interest statement:

None to declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Abstract

Background/Aim: Tooth autotransplantation has been advocated for replacement of missing teeth, or teeth that are unsuitable for restoration. The aim of this study was to investigate the outcomes and prognostic factors that influenced the success of tooth transplantation in a paediatric population.

Materials and Methods: Data was extracted from the records of 75 patients (89 teeth). Demographic and prognostic factors were recorded and analyzed for the clinical and radiographic outcomes for periodontal ligament (PDL) and pulp healing of transplanted teeth.

Results: The mean age at transplant was 13.2 years and the mean follow-up observation period was 2.6 ± 1.8 years with a range of 12.0 months-9.9 years. The main reason for transplantation was to replace upper central incisors lost or missing due to dental trauma, hypodontia and dilaceration. Of the 45 teeth that were monitored for pulp revascularization, 75.6% showed clinical and radiographic signs of pulp healing and 24.4% showed signs of pulp necrosis and infection. Pulp healing was significantly related to the stage of root development of the transplant. Favourable PDL healing was observed in 87.6% of the transplants, while 13.5% showed signs of replacement resorption. PDL healing was significantly related to the stage of root formation of the transplanted tooth at the time of the surgery, the ease of handling and placement of the tooth, and the status of the alveolar bone at the recipient site at the time of the surgery. Overall success of tooth transplantation was 87.6% and the survival rate was 94.4%.

Conclusions: Tooth transplantation carried out in children and adolescents demonstrated high success and survival, with the stage of root development influencing both the pulp and PDL healing of the transplanted teeth.

Introduction

Tooth autotransplantation has been advocated for the replacement of missing teeth and teeth that are unsuitable for restoration, as well as for treating certain orthodontic problems.^{1, 2} Tooth transplantation is indicated in growing patients with missing teeth due to trauma or agenesis, or with teeth with a poor survival prognosis in the long-term, where an appropriate donor tooth can be used without negative effects in the arch.^{3, 4} Interest in this procedure has

been revived because it has been shown to provide functional adaptation, alveolar bone induction, preservation of the alveolar bone ridge and re-establishment of a normal alveolar process.⁴

Resorption of bone from the alveolar process after traumatic loss of permanent teeth creates a challenge for the replacement of missing teeth and for prosthetic rehabilitation. The volume of the alveolar bone decreases significantly following extraction or loss of a permanent tooth from the dentition. In many cases when the time comes to consider implants, bone augmentation is frequently required before this can be accomplished. Therefore, it would be preferable to provide treatment that can maintain bone and adapt to both growth and developmental changes.^{1, 5} Autotransplantation however does carry risks of potential unfavourable outcomes, which include pulp necrosis and infection, replacement resorption and lack of root development among others. Few studies have been published reporting the success and survival of transplanted teeth in children and adolescents.^{1, 6, 7}

Tooth transplantation has been carried out in the Leeds Dental Institute for the last 12 years and has been organised through an interdisciplinary environment with integrated planning undertaken by orthodontists and paediatric dentists. Each patient is assessed with the view to considering the immediate, short term and long term outcomes, as well as alternative treatment options. It is hoped that such an interdisciplinary approach enhances the outcomes for autotransplantation in children and adolescents.

Therefore, the aims of this study were:

- (i) To evaluate the outcomes of tooth transplantation in a paediatric population at the Leeds Dental Institute for pulp and periodontal ligament healing.
- (ii) To evaluate the level of success and survival of the autotransplanted teeth.
- (iii) To identify the prognostic factors which influenced the outcomes of pulp and periodontal ligament (PDL) healing.

Materials and Methods

The study sample was selected from the clinical dental records of paediatric patients treated at the Leeds Dental Institute. Patients who underwent tooth transplantation procedures under local or general anesthesia were included in the study. This was a retrospective study involving patients notes. For this type of study formal consent from the patients was not

required. Full compliance with data protection and safeguarding of data was ensured and no information which could identify the patients was collected.

The Clinical Dental Records (CDR) were selected to be included in the study according to the following criteria:

- Patients attending the paediatric dental clinic of the Leeds Dental Institute following referral for diagnosis, treatment plan and treatment for tooth transplantation.
- Patients aged up to 16 years old by the time the surgery was carried out.
- Patients who had one or more missing or a tooth requiring extraction, for which a transplant had been carried out.
- Minimum of 12 months follow-up period post-surgery at the Paediatric Dental Department of the Leeds Dental Institute.

Clinical and radiographic data was collected retrospectively from the CDR. To ensure consistency in data extraction, the clinical and radiographic records of the first 30% of cases were reviewed by two examiners for training purposes. Inter-examiner reliability was evaluated to ensure agreement between both examiners and that the indices were used consistently. Final data extraction was conducted by a single calibrated examiner using a standardized data extraction proforma.

The clinical findings were identified as recorded in the dental records by the clinicians who had reviewed the patient during the follow-up observation period. Recorded clinical data that was identified included:

- Demographic factors,
- Relevant prognostic factors at the time and immediately after transplantation,
- Outcome measures at the 12-month review visit,
- Outcome measures at the latest recorded follow-up visit,
- Number of treatment visits in the Paediatric and Orthodontic Clinics.

The radiographs were assessed by the main examiner who had been trained and calibrated. In the event of discrepancies between the recorded findings and the examiner's assessment of the radiographs, a second opinion was sought from another examiner and a decision on the final outcome was achieved through consensus after discussions.

The rest of the cases were reviewed by the one examiner only. Wherever there was a query regarding either a clinical or radiographic finding, the opinion of the second examiner was requested in order to reach a common consensus.

The following variables which may influence the prognosis of the autotransplanted teeth were recorded:

1. Donor tooth
 - Tooth type
 - Eruption status: unerupted, partially erupted or fully erupted
 - Stage of the root and apex development: divergent, parallel, convergent with open apex, and closed apex.⁸
2. Recipient site and surgery
 - Position of the recipient site
 - Alveolar bone status at recipient site: adequate or deficient bone level
 - Surgical difficulty and ease of placement of the autotransplant
3. Method of tooth stabilisation post-transplantation
4. Endodontic treatment: timing of treatment initiation and technical quality of the root canal filling (based on radiographic appearance)
5. Cause of tooth loss that necessitated treatment with an autotransplant: e.g. trauma, hypodontia, dilacerations, caries etc.

The type of healing response was assessed based on both clinical and radiographic evaluations. The following criteria were considered:

(a) Clinical

- Periodontal ligament (PDL) healing - defined as a tooth having normal (physiological) tooth mobility, and normal percussion sound. Any pathological mobility or high metallic percussion sound was considered to be unfavourable healing indicative of ankylosis.
- Pulp healing - defined as a positive response to pulp sensibility testing (either electric or cold/thermal stimuli), absence of tenderness to percussion, and absence of signs or symptoms of pathosis such as abscess, swelling or sinus tract.

(b) Radiographic

- PDL healing- defined as a tooth with presence of continuous PDL space and intact lamina dura surrounding the entire root periphery. Radiographic presence of periapical radiolucency and loss of lamina dura or widening of the PDL space were indicative of unfavourable healing. Any signs of ankyloses and/or related replacement resorption were recorded as unfavourable healing. Surface resorption (repair related) or infection-related (inflammatory) resorption that had been treated effectively with endodontic treatment was considered favourable. The presence of root resorption was evaluated from the radiographs according to the classification used by Andreasen and Hjorting-Hansen (1966).⁹⁹
- Pulp healing – Diagnosis of pulp healing was made if partial pulp canal obliteration or continued root formation was evident. An absence of response to pulp sensibility tests was disregarded if clear evidence of pulp healing could be determined from the radiographs, such as observation of continued root development or pulp canal obliteration in the first 6 months following transplantation. Pulp necrosis and infection was considered to have occurred when transplanted teeth presented radiographically with a periapical radiolucency or infection-related resorption, with or without a response to pulp sensibility testing and other symptoms of pulp necrosis as evaluated by the clinicians. In the absence of positive pulp sensibility test results, pulp necrosis and infection was assumed in situations where the pulp canal showed no signs of obliteration or continued root development 6 months after transplantation. Pulp canal obliteration was recorded from the radiographs available according to the classification of Jacobsen and Kerekes (1977)

- Peri-radicular region – This was undertaken as described by Paulsen and co-workers.⁶ Peri-radicular regions were evaluated as normal when the PDL space was present with a normal width and lamina dura was intact. Pathosis was recorded when changes were present in the PDL space, from widened to marked radiolucent areas.

For the purposes of this study, the following criteria were used to record a final outcome of the autotransplantation:

(i) Success:

- Teeth with immature root formation that had pulp revascularization following transplantation.
- Successful endodontic treatment performed (with absence of periapical pathosis) in teeth with necrotic immature teeth and in teeth with complete root development in which the pulp was electively removed following transplantation.
- Favorable periodontal healing with either no evidence of external root resorption or where the resorption was effectively treated and controlled with endodontic treatment.
- Normal alveolar bone process.

(ii) Survival:

- Replacement resorption (ankylosis), Unfavorable PDL healing with the tooth still present in its transplanted position at final follow-up visit

Data analysis was performed using SPSS 17.0 software (IBM SPSS Statistics). Descriptive statistics including means, medians and ranges were computed. Univariate analysis was performed using Chi-Square or Fisher's Exact Test to investigate associations between the prognostic factors and the outcome measures of pulp and PDL healing. A value of $p < 0.05$ was considered to be statistically significant. The statistical analysis for the relationship between the pulp and PDL healing and the prognostic factors was carried out on a subject level, where one tooth only was randomly selected from each subject.

Results

A total of 89 autotransplanted teeth in 75 patients (46 males and 29 females) were included in this study. The mean age of the patients at the time of the surgery was 13.2 years \pm 2.0 years (range 9.0-16.0 years). The majority of the autotransplantation procedures were carried out under general anesthesia and were placed in the upper anterior area (94.4%). The most frequent reason for tooth transplantation was secondary to dento-alveolar trauma in the permanent dentition (81.1%), followed by hypodontia (11.1%). The most common donor teeth were premolar teeth (92.0%), with the upper second premolar being used as a donor tooth in approximately half of the cases. Most of the donor teeth were fully erupted at the time of transplantation. The mean observation period was 2.6 \pm 1.8 years and ranged from 12 months to 9.9 years.

Favourable PDL healing was recorded for 79 (87.6%) of the autotransplanted teeth, of which 65 teeth had no root resorption, and 10 teeth had repair related surface resorption. Infection-related resorption and replacement resorption (unfavourable healing) accounted for 2.2% (n=2) and 13.5% (n=12) teeth respectively (Table 1).

Forty five teeth transplanted in 75 subjects had a divergent, parallel or convergent root form with open apices, and therefore they were considered to have a chance for pulp revascularization, and were monitored for pulp healing after surgery. Overall pulp survival was 75.6%, with 34 autotransplanted teeth showing signs of pulp healing (Figure 1). The other 11 teeth presented with pulp necrosis and infection for which root canal treatment had been adequately provided.

The final success and survival rates of autotransplanted teeth included in the study was 85.4% and 94.4% respectively as determined by both clinical and radiographic evaluation of teeth at the last follow-up visit.

Analysis of the correlation between the prognostic factors and pulp and PDL healing was carried out on a subject level, where one tooth only was randomly selected from each subject and included in the analysis. The results are therefore presented for 75 subjects for the periodontal healing and for 39 subjects for pulp healing where teeth had been replanted with divergent, parallel and convergent root development and pulp healing was considered a possibility.

(i) Pulp healing

Pulp healing was found to be significantly related to the stage of the root development (Table 2). Significantly more teeth with divergent and parallel apical root development demonstrated pulp healing compared to those with convergent roots. Teeth with completed root development where no pulp healing was expected to occur were excluded from this analysis, and elective endodontic treatment was initiated after surgery. Pulp healing was not significantly related to any other recorded prognostic factor.

(ii) PDL and stage of root development

Favourable PDL healing was statistically significantly related to the stage of root development ($p < 0.001$), the surgical difficulty, and the ease of handling and placement of the graft, and the status of the alveolar bone at the recipient site ($p < 0.001$).

In order to study the effect of the stage of root development on the PDL healing, teeth with open apices which were in the divergent and parallel groups were combined and categorized as being “immature” teeth, and teeth with convergent roots with open apices and complete root development were categorized as having “mature” root development. There was a significant difference in favourable PDL healing outcomes between immature and mature roots ($p < 0.001$) (Table 3).

(iii) PDL healing and ease of donor placement at recipient site

The handling and placement of the graft at the recipient site was found to significantly affect PDL healing outcomes ($p < 0.001$), with significantly better outcomes for teeth in which the graft placement was easy compared to difficult cases. (Table 4)

(iv) PDL healing and status of alveolar bone at recipient site

The alveolar bone status at the recipient site had a highly significant effect ($p < 0.001$) on the outcome of PDL healing. Teeth that were placed in areas of no bone deficiency demonstrated higher levels of favourable PDL healing.

Discussion

The present study investigated the pulp and PDL healing of transplanted teeth in a paediatric population and its associations with various prognostic factors. Clinical and radiographic parameters are commonly used in the evaluation of “success” in autotransplantation studies. Definitions of success and survival were based on the criteria established and used in previous studies.¹⁰⁻¹² In this study, biological factors that affect the outcome of transplantation such as pulp and PDL healing, as well as the presence or absence of external root resorption were used as the main outcome measures to define treatment success. Of these, PDL healing is considered as the key factor as this affects the long-term prognosis of the transplanted tooth. The rationale for this is that should pulp healing fail to take place, effective endodontic management can still ensure a good outcome for the tooth. However, if unfavourable PDL healing occurs, the long term prognosis and hence tooth survival will be compromised.

The mean age of the subjects at the time of the transplantation was 13.24 ± 2.0 years. The completion of root development for the first and second premolars occurs between 12-14 years of age.¹³ This is an ideal time for autotransplantation as the premolar would have erupted, and attained adequate root length with a favourable crown-root ratio, while still having a sufficiently open apex to facilitate revascularization and pulp healing. The stage of root development of the transplanted tooth was found to be one of the most important factors affecting the outcomes for both pulp and PDL healing in this study.

Cases with a follow up period of less than 12 months were excluded from the study. This was because the authors felt that a minimum period of 12 months was required for pulp and PDL healing to be observed. In this study, 39 of 75 teeth had open apices with a chance of achieving pulp healing. Of these, 76.9% (n=30) showed signs of pulp revascularization. This compares favourably with previous studies reported in the literature.^{6, 12, 14-16}

Partial pulp canal obliteration and continued root development were the key factors used to diagnose pulp survival. Early radiographic signs of partial pulp canal obliteration were identified in 73.5% of the cases that demonstrated revascularization at the 6-month review, with 100% presenting with pulp canal obliteration in the first 12 months following transplantation. These figures concur with earlier investigations that show radiographic signs

of pulp canal obliteration within 6 months after surgery.^{6, 12, 14, 15} Placwicz et. al. (2013) reviewed 23 cases and reported pulp healing in most of their sample, with improved crown : root ratios over time, signifying continued root development with pulp canal obliteration in several cases.¹⁷

Of the prognostic variables evaluated, pulp healing was found to be significantly associated with the stage of root formation at the time of transplantation with significantly higher chances of pulp healing when the root development was immature (divergent and parallel stage). A previous study by Andreason and co-workers correlated the size of the apical foramen with pulp healing,¹⁴ in which the authors concluded that a diameter above 1mm had a low risk of pulp necrosis. Stages 3 and 4 of root development¹⁸ can be correlated with the 'divergent' and 'parallel' groups in this current study. Revascularization is more predictable for teeth with wider apices than those with narrower apices and mature roots. During autotransplantation, severance of the vascular and nerve supply to the pulp occurs. With this, serious damage occurs to both the architecture and function of the pulp during the surgical procedure.¹⁹ Following transplantation, healing occurs through revascularization with restoration of the pulp including the blood and nerve supply. Consequently, teeth with incomplete root formation teeth have a better chance for revascularization due to increased vascularity related to the wider open apices.¹⁴ This concurs with a recent systematic review²⁰ which reported that although the quality of studies were poor, it could be reasonably concluded that the stage of root development was correlated to the success of the procedure.

There was excellent PDL healing for the teeth monitored in this study, with very few teeth showing signs of root resorption which was either not self-limiting or controlled with endodontic intervention. This finding is similar to several other studies.^{1, 14, 17, 21, 22} In the current study, the stage of root development was found to be significantly related to the PDL healing, with all the unfavourable cases in this study being those where root development was complete. However, the majority of cases with complete root development in this study demonstrated favourable healing. This is consistent with that reported in a recent systematic review²³ which assessed clinical outcomes for autotransplanted teeth with complete root formation, and found that the outcomes were largely favourable with root resorption and ankylosis being rare.

PDL healing was favourable in all cases where the handling and placement of the graft was recorded as 'easy' compared to the group where it was 'difficult', where all unfavourable outcomes were seen. Trauma to the PDL has been reported as the main factor associated with non-favourable PDL healing of transplanted teeth,^{6, 14, 24} and a prolonged and difficult surgical procedure would contribute to increased stress to the periodontal ligament. This is also related to the quality of the bone at the recipient site, and where bone is deficient, the surgical procedure tends to be more difficult. An anecdotal observation in this current study was that most of the unfavourable outcomes were cases that were done very early in the transplantation programme as the surgical techniques were refined over a period of time. Surgery carried out by an experienced operator with the necessary surgical skills with respect to the handling of tissues (both the pulp and PDL), would have an influence on the ease of placement of the graft and therefore the outcomes. Previous studies have shown the importance of an experienced operator for successful outcomes for autotransplantation.^{11, 14, 15} Unfavourable PDL healing has been shown to be significantly related to damage to the innermost layer of the periodontal ligament.^{25, 26} During extraction and handling of the donor tooth, care must be taken to minimize damage to the PDL close to the root surface and also to avoid compression of the PDL. Damage to these sensitive fibres during extraction of the donor tooth plus prolonged handling and extra-alveolar time during surgery can cause damage to the cementum, making it more vulnerable to osteoclastic activity.

The status of the alveolar bone at the donor site was also significantly associated with favourable PDL healing. No previous study has reported this as a prognostic factor, although from a clinical perspective it does seem to be an important consideration. Both the bucco-palatal and the vertical height of the bone are important clinical variables as they enable the transplanted tooth to be placed in an area of good quality bone with sufficient thickness which promotes a good healing outcome for the PDL. Additionally, adequate vertical bone height would result in better aesthetic outcomes. In this study, most of the cases had adequate bone levels as within the interdisciplinary planning, care was taken to maintain bone levels at the recipient site, and procedures such as decoronation were carried out wherever required in a timely manner. However, late presentation is sometimes inevitable as referrals can sometimes be delayed to the Specialist Centre in which case atrophy of the bone may have already occurred.

A systematic review²³ indicated that the administration of antibiotics, type of splinting (sutures alone versus wire-composite splinting) and the timing of endodontic treatment had a significant correlation with outcomes of autotransplantation. In this present study, the results did not show any effect of these variables on the healing of either the pulp or the PDL. This may be attributed to the standardized protocol that was implemented for all autotransplantation cases carried out at the Leeds Dental Institute, to which all operators were trained and calibrated. All children received antibiotics at the time of surgery, and splinting was carried out with a flexible titanium splint, with endodontic treatment commencing within 14 days of the surgery for mature teeth.⁵ Although some have questioned whether autotransplantation should be carried out once the donor tooth has completed root development, it has been shown in this study that transplanted mature teeth with adequate root canal treatment following surgery have a good prognosis, which is in agreement with previous studies.^{1, 15}

Although a small percentage of the teeth in this study did show signs of ankylosis and replacement resorption, these teeth can still serve an important role in maintaining bone in this site for the future. Atrophy of bone in edentulous sites is inevitable, often requiring bone augmentation before an implant can be placed. In this study, autotransplants that were deemed to be unfavourable due to ankylosis, could be decoronated in order to preserve both the bucco-palatal width and the vertical height of the bone in that region to facilitate the placement of an implant without requiring bone augmentation.

Most of the autotransplants in this study were carried out in the maxillary anterior region and were intended to replace permanent incisors lost due to either avulsion or following ankylosis-related root resorption. Traumatic injuries to the permanent incisors such as avulsions and intrusions often lead to subsequent ankylosis-related resorption and a poor long-term prognosis.²⁷ Transplantation in such cases offers a biological replacement for the patients.

All the autotransplantation cases undertaken at the Leeds Dental Institute were planned in consultation with an interdisciplinary team, including paediatric dentists and orthodontists amongst others. Following severe trauma such as avulsion or intrusion where ankylosis and infra-occlusion are likely, the care of such patients is overseen by the team, with timely management of infra-occlusion with procedures such as decoronation. This in turn preserves the integrity of the alveolar bone in the recipient site, a variable found to have a significant

influence on PDL healing. Most cases included in the current study had autotransplants placed in recipient areas where no bony deficiency had been recorded, which in many cases is directly a result of the timely execution of bone conserving procedures such as decoronation. Treatment planning for these cases commences at the stage where the poor prognosis of the existing tooth is first detected. At this juncture, pre-operative bone management protocols (e.g. decoronation) are put in place where required, with orthodontic treatment and autotransplantation surgery commencing at appropriate times, followed by careful and close post-operative endodontic monitoring, and treatment as necessary. This is likely to have contributed towards the high success rates reported in this present study.

Conclusions

The replacement of teeth with tooth autotransplantation had excellent outcomes in children and adolescents, with most transplanted teeth demonstrating excellent PDL healing with no external root resorption. Over two thirds of the donor teeth which had incomplete root development at the time of autotransplantation demonstrated pulp healing and continued root development, with the stage of root development having a significant influence on both the pulp and PDL healing.

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Table 1. The number of autotransplanted teeth that presented with different types of root resorption.

Resorption	Frequency	Percentage
No Resorption	65	73%
Repair related (surface)	10	11.2%
Infection related (Inflammatory)	2	2.2%
Replacement	12	13.5%
Total	89	100%

Table 2: Pulp healing related to the stage of root development of the autotransplanted teeth that were monitored for pulp revascularization

		Divergent	Parallel	Convergent	Total
Pulp Healing	Yes	12**	16**	2	30
	No	0	2	7	9
Total Number of subjects		12	18	9	39

*subject level analysis; teeth with complete root development excluded from analysis.

**Pearsons Chi Square $P < 0.05$

Table 3. Comparison of PDL healing between immature ('divergent' and 'parallel') and mature ('convergent' and 'complete') root development.

		Immature	Mature	Total
PDL healing	Favourable	31**	34	65
	Unfavourable	0	10	10
Total number of subjects		31	44	75

*subject level analysis, **Fisher exact test $P < 0.05$

Table 4. PDL healing related to surgical difficulty and ease of donor placement at the recipient site*.

		Easy	Difficult	Total
PDL healing	Favourable	49**	16	64
	Unfavourable	0	10	10
Total number of subjects		49	26	75

*subject level analysis, **Fisher exact test $P < 0.05$

Table 5. PDL healing related to the alveolar bone status at the recipient site*.

		No Deficiency	Bone Deficiency	Total
PDL healing	Favourable	57**	8	10
	Unfavourable	3	7	64
Total number of subjects		60	15	75

*subject level analysis, **Fisher exact test $P < 0.05$

