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SURVIVAL OF AUTOTRANSPLANTED TEETH WITH OPEN APICES, A RETROSPECTIVE COHORT STUDY

Juslin Jessica, Jääsaari Päivi, Teerijoki-Oksa Tuija, Suominen Auli, Thorén Hanna

ABSTRACT

Purpose:

Autotransplantation of teeth is an alternative treatment method in growing patients suffering from hypodontia or impacted teeth. The purpose was to investigate the occurrence of and predictors for the loss of transplanted teeth in children and young adults.

Methods:

All patients who had undergone tooth transplantation at the Department of Oral and Maxillofacial Diseases, Turku University Hospital during the time period October 1st 2009 and January 5th 2017 were identified from the hospital´s database. The outcome variable was the survival of the transplanted tooth. The predictor variables were the type of transplantation, the donor tooth, the maturity of the donor tooth, the number of roots of the donor tooth, the recipient's jaw, the need for extra-oral storage of the donor tooth during surgery, continuation of root development during follow-up and institution experience. One tooth was randomly selected from each subject. The Kaplan-Meier method of survival analysis and the Cox proportional hazards regression analysis were used to assess the association between survival and risk factors

Results:

The sample was composed of 36 subjects with a mean age of 14.3 years and 33.3 % were male. 45 teeth were transplanted, the median follow-up time was 1.3 years. The one-year survival rate was 87% (95% CI: 75-99%). A significant predictor for tooth survival was the continuation of root development (HR=21.3; 95% CI: 2.1-215.0; p=0.009). Although not statistically significantly, more favorable prognoses were for distant than transalveolar transplantations, for one-rooted than multi-rooted teeth, for premolars than molars, for teeth not stored in an extra-oral media, and for teeth that had been transplanted later during the study period.

Conclusion:

Experience of the professional team, use of open apex premolars and postsurgical continuation of root development of the transplant are factors that associate with a favorable outcome. Transplants could benefit from the use of 3-dimensional replicas during surgery .

INTRODUCTION

In tooth transplantation, a donor tooth is surgically removed and positioned in a recipient area of the same individual. Most often the patients going through tooth transplantation are growing children and adolescents, and in some circumstances young adults. Common indications for tooth transplantation are impacted teeth, congenitally missing teeth and tooth loss due to trauma, caries or malformation [1].

For growing patients, transplants need to adapt to the ongoing changes during growth of a young individual and also adapt to the developing occlusion. For an aesthetically and functionally good outcome it is important that the alveolar bone is preserved and that the bone enveloping the area of the transplanted tooth continues to grow vertically. Because of vertical bone growth, it is problematic to replace missing teeth with dental implants in

growing individuals, whereas a transplanted tooth is able to preserve the alveolar bone [1-4] allowing root development and eruption of the donor tooth [2,5,6]. After surgery, the position of the transplanted tooth can be modified by orthodontics [3,4].

Several factors can affect the success of the transplant. The transplanted tooth can survive only if the vascular and nerve bundles in the apical area and the periodontal ligament (PDL) recover after surgery [3,7]. Specific factors potentially affecting treatment success are, among others, root morphology, stage of root development, and various factors related to the surgical procedure [7-14]. In addition, patient satisfaction is a relevant measure of success [15,16].

The purpose of the present study was to clarify survival of transplanted teeth in children and young adults, and to identify risk factors associated with loss of transplanted teeth. The hypothesis was that one or more factors associated with the loss of transplanted teeth could be modified by the clinician to improve survival.

PATIENTS AND METHODS

Study design

To address the research aims, a retrospective cohort study was designed and implemented. All patients who had undergone tooth transplantation at the Department of Oral and Maxillofacial Diseases, Turku University Hospital during the time period October 1st 2009 and January 5th 2017 were identified from the hospital´s database.

Study variables

All the study variables (outcome and predictor variables) are listed in Table 1.

Outcome variable

The outcome variable was survival of the transplanted tooth.

Predictor variables

The type of transplantation was defined as either distant or transalveolar. In distant transplantation, the donor tooth was removed and transplanted to a distant site, and stabilized with sutures or a wire splint. In transalveolar transplantation, the donor tooth was transplanted in its own location to a more ideal position and fixed with sutures or a wire splint [17].

The tooth type was defined as premolar or molar and the number of roots of the donor tooth was defined as single- or multi-rooted.

The maturity of donor teeth were defined and classified into stages A-H according to Demirjian et al[18]. In stages A to D, the crown was either forming or fully formed. In stages E to G the root was forming and the apex was open. In stage H, the tooth was fully formed and the apex was closed.

The recipient jaw was either mandible or maxilla.

Extra-oral storage of the donor tooth either occurred or did not occur during surgery.

Continuation of root development was established when the length of the root continued to increase and/or the apex closed during the follow-up period.

In order to classify the institution experience, the transplanted teeth were defined as early transplantations (performed during the years 2009-2014) and as late transplantations (performed during the years 2015-2017).

Data analysis

Statistical analysis was performed on subject level, where one tooth was randomly selected from each subject and included in the analysis.

We used the Kaplan-Meier method of survival analysis to describe the survival of the transplanted tooth and the Cox proportional hazards regression analysis to assess the association between survival and risk factors. Kolmogorov-type supremum test was used to verify the assumption of stable hazards ratios across follow-up time.

Statistical analyses were performed with SAS version 9.4 for Windows (SAS Institute Inc., Cary, NC, US) and SPSS Statistics version 25 for Mac (IBM). Results with p-values <0.05 were considered statistically significant.

Ethical considerations

The Internal Review Board of the Hospital District of South-Western Finland approved this study.

RESULTS

Survival of transplanted teeth

The sample was composed of 36 subjects with a mean age of 14.3 years (range 9.8-22.9 years) and 33.3 % were male. Altogether 45 teeth were transplanted, the median follow-up being 1.3 years (range 0.1-5.3 years). Twenty-nine of the 36 patients had been followed up for at least 1 year.

Table 2 shows descriptive statistics of the total of 45 transplanted teeth in 36 patients as well as of those 36 randomly chosen teeth that were included in the statistical analysis. Of the total of 45 teeth, eruption failure was the most common cause of transplantation (n=21). In all transplanted teeth, the root was still forming and the apex was open. Distant transplantations

were more common (n=29) than transalveolar (n=16), the most frequent recipient jaw being the mandible (n= 29). 13 teeth needed to be stored extra-orally in saline, blood or their mixture. All patients received antibiotics preoperatively.

As shown in Table 3, of the 45 transplanted teeth, the most common donor tooth was the maxillary 2nd premolar (n=17) and the most common recipient dental areas were the mandibular 2nd molar (n=13) and maxillary 2nd premolar (n=11).

Of totally 45 transplanted teeth, 8 were lost during the study period, giving an overall survival prevalence of 82 %. The one-year survival rate was 87% (95% CI: 75-99%), see Figure 1a. Reasons for tooth loss were unsatisfactory position of the transplant (n= 3), root resorption (n= 2), pulp infection (n= 2) and ankylosis (n= 1). In the cases of unsatisfactory position of the transplant, the tooth situated poorly in the transversal dimension compared to the dental arch or in the vertical dimension compared to the occlusal plane.

Table 4 shows the survival prevalence per donor tooth and per recipient dental area. Third molars had the lowest the survival rates being 71% for maxillary and only 57% for mandibular third molars. The recipient dental area with the lowest survival rate was that of the lower second molar (62%).

Table 5 shows the association between 36 randomly chosen teeth and the predictor variables. The only significant predictor for tooth survival was the continuation of root development (p=0.009). Patients with a transplanted tooth with discontinued root development were 21.3 times as likely to lose the transplant, as were patients with a transplanted tooth with continued root development. However, we have to interpret it with some caution due to the broad confidence interval.

Figure 1 (b.-i.) shows the Kaplan-Meier survival curves for each predictor. Although not statistically significant, the prognoses were more favorable for distant than transalveolar transplantations, for premolars than molars, for one-rooted than multi-rooted teeth, for teeth that had not been stored in extra-oral media, and for teeth that had been transplanted later during the study period.

DISCUSSION

The purpose of the present study was to clarify survival of transplanted teeth in children and young adults, and to identify risk factors associated with loss of transplanted teeth. The hypothesis was that one or more factors associated with loss of transplanted teeth could be modified by the clinician to improve survival.

The results revealed a survival prevalence of 82 % of 45 transplanted teeth in 36 patients. In The one-year survival ratio was 87% (CI: 75-99%). In the statistical analysis of the 36 randomly chosen teeth, the predictor, which improved survival statistically significantly, was the continuation of root development (p=0.009). In these 36 teeth, factors associated with lower survival rates, although not statistically significantly, were molars (80 %), multi-rooted teeth (83,3 %), and teeth that had been stored extra-orally during surgery (72,7 %). The average survival rate improved over time with increasing experience from 77,8 % to 94,4 %.

The authors of recently published meta-analyses have shown that the overall success and survival of transplanted teeth in general is high [7,14,19]. However, the studies approved for the meta-analyses revealed a notable dispersion of survival rates (75%-100%), as well as success rates (90%-97%). As there are numerous potential factors that may influence outcome, the discrepancy in results most likely reflects the heterogeneity between studies regarding predictors.

As shown in the meta-analysis by Almpani et al [8], teeth with open apices were less likely to be lost as the risk of extraction need decreased by 70% (RR=0.3, 95% CI=0.2-0.6) compared to teeth with closed apices. The roots of all transplants included in the present study were still forming and the apices were open at the time of surgery. However, in closer analysis we could not find an association between the stage of root maturity and survival.

In this study the prognostic factor that associated most strongly with survival was the continuation of root development (HR=21.3; 95% CI: 2.1-215.0; p=0.009). From earlier studies [3,] we know that continuation of root growth can be anticipated after transplantation. The part of the root that was formed before the time of operation shows pulp obliteration, whereas the part formed during the follow-up often has a normal pulp chamber[4]. This is illustrated in Figure 2a and 2b. The obliteration of the root canal and continuation of root development suggests that the transplanted tooth has remained vital. Arrest of root development occurs when the Hertwig's epithelial root sheath is damaged during the extraction or fitting of the transplant [3]. In this study, 96,3 % of the teeth that had continued root formation, where still functioning during the follow-up period.

The one-year survival rate of 87 % observed in the present study settles at the lower end of rates that have been reported previously in studies focusing on teeth with incomplete root development [14,19]. One reason likely derives from the fact that multi-rooted teeth in general (23/45), and molars in particular (20/45) were frequently used in our patients. One unsuccessful patient case is shown in Figure 3. These transplants showed low survival prevalence of 74% and 70%, respectively. Previously it has been shown that premolars have a significantly more favorable prognosis than molars [14], which was also confirmed in the present analysis; 95% of transplanted premolars survived.

The present study demonstrates the well-known fact that surgical success increases with increasing experience of the team of professionals. The average survival prevalence increased by 17 percentage points when the early transplantation group was compared to the late transplantation group. Careful selection of patients, meticulous patient information, close collaboration between the orthodontist and the surgeon, and standardized treatment and follow-up protocols are of outmost importance. In Figure 4 we show a successful patient case of transalveolar transplantation of maxillary canines.

Regarding the surgical procedure in particular, delicate handling of the transplant is required in order to maintain the health of the periodontal ligament. Moreover, the root surface should not be allowed to dry [20,21] as drying initiates osteogenesis in the alveolar bone, which further predisposes for ankylosis [20]. In our patients, saline, blood or their mixture was used as storage media for those 13 transplants that had to be stored extra-orally during the procedure. Despite this, three of the transplants did not survive. Due to the retrospective nature of the present study, we were not able to state the exact duration of the extra-oral time that occurred during surgery. However, in a study of Jang et al[22], regarding survival of teeth in intentional transplantation, teeth in which extra-oral time was under 15 minutes or less were more successful than those with extra-oral time for more than 15 minutes.

The need for extra-oral storage reflects another relevant mechanism for PDL damage, namely multiple transplant fittings of the donor to its new alveolus, which further increases the risk for transplantation complications [7]. Due to the retrospective nature of the present study, we were not able to analyze the influence of the degree of transplant manipulation on the outcome. However, we may assume that multi-rooted teeth and molars were exposed to more manipulation on average than one-rooted teeth and premolars, highlighting perhaps the most relevant explanation for poor survival of molar transplants.

The use of a 3-dimensional replica could potentially help surgeons decrease the challenges associated with autotransplantation. Extra-oral time and the degree of manipulation of the donor tooth are factors that could potentially be modified by using patient specific donor tooth replicas. Shahbazian et al. [23] performed a case-control study of 40 pediatric patients, comparing the outcome of conventional autotransplantation with the use of stereolithographic tooth replicas and surgical guides. The use of tooth replicas resulted in reduced surgical and extra-alveolar time as well as less need for manipulation of the donor teeth. The prognosis of multi-rooted teeth and molars in particular could potentially benefit from the use of replicas. The replica might potentially provide extra guidance for surgeons who are not that experienced with tooth transplantation. This topic has gathered increasing interest in recent years [24,25] and should be investigated further. To our knowledge, randomized prospective clinical studies about this subject have not been published yet.

CONCLUSIONS

Tooth transplantation is a valuable treatment option in children and young adults. The experience of the professional team, the use of open apex premolars, and the postsurgical continuation of root development of the transplant are factors associated with a favorable outcome. Poor survival rates are associated with molars, which are presumably more frequently exposed to multiple fitting trials and manipulation than premolars. The prognosis of transplants in general and multi-rooted transplants in particular could benefit from the use of 3-dimensional replicas during surgery. Further high-quality prospective randomized clinical trials are required in this field of interest.

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Table 1. The study variables*

Outcome Variable	
	The survival of the transplanted tooth
Predictor Variables	
	1. The type of transplantation
	2. The donor tooth
	3. The maturity of the donor tooth
	4. The number of roots of the donor tooth
	5. The recipient jaw
	6. The need for extraoral storage of the donor tooth
	7. Institution experience
	8. Continuation of root development

* Please see the Patients and Methods section for a further description of the study variables

Table 2. The descriptive statistics of the total 45 transplanted teeth in 36 patients, and of the 36 teeth that were included in the statistical analysis

	Number of teeth (=45)	Number of teeth included in statistical analysis (=36)
The year of the transplantation		
2009	1	1
2012	8	6
2013	2	1
2014	11	10
2015	11	9
2016	11	8
2017	1	1
The use of perioperative antibiotics		
Yes	45	36
The reason for the transplantation		
Eruption failure	21	16
Congenitally missing	13	12
Malposition	8	5
Dental decay	2	2
Traumatic loss	1	1
The maturity of the donor tooth *		
E	6	5
F	31	24
G	8	7
The type of transplantation*		
Distant	29	26
Transalveolar	16	10
Type of the donor tooth		
Premolar	22	19
Molar	20	15
Canine	3	2
The number of roots of the donor tooth		
Single-rooted	22	18
Multi-rooted	23	18
The recipient jaw		
Mandible	29	25
Maxilla	16	11
The need for extraoral storage of the donor tooth		
No	32	25
Yes	13	11
Continuation of root development*		
Yes	34	28
No	11	8

* Refer to the Patients and Methods section for the definitions of the study variables

Table 3. Donor teeth and recipient dental areas in the 36 patients

	Number of teeth (=45)	Number of teeth included in statistical analysis (=36)
The donor tooth		
Maxillary 2nd premolar	17	14
Maxillary 3rd molar	7	5
Mandibular 3rd molar	7	5
Mandibular 2nd molar	6	5
Maxillary 1st premolar	3	3
Maxillary canine	2	1
Mandibular 2nd premolar	1	1
Mandibular 1st premolar	1	1
Mandibular canine	1	1
The recipient dental area		
Mandibular 2nd molar	13	9
Maxillary 2nd premolar	11	8
Mandibular 2nd premolar	9	9
Mandibular 1st molar	5	5
Maxillary canine	2	1
Maxillary incisor	1	1
Maxillary 2nd molar	1	0
Maxillary 1st premolar	1	1
Mandibular 1st premolar	1	1
Mandibular canine	1	1

Table 4. The **survival prevalences** for the transplanted donor teeth and the recipient dental areas

	Survival prevalence
Total	82 %
The donor tooth	
Mandibular canine (n=1)	0 %
Mandibular 3rd molar (n=7)	57 %
Maxillary 3rd molar (n=7)	71 %
Mandibular 2nd molar (n=6)	83 %
Maxillary 2nd premolar (n=17)	94 %
Maxillary 1st premolar (n=3)	100 %
Maxillary canine (n=2)	100 %
Mandibular 2nd premolar (n=1)	100 %
Mandibular 1st premolar (n=1)	100 %
The recipient dental area	
Mandibular canine (n = 1)	0
Mandibular 2nd molar (n = 13)	62 %
Mandibular 1st molar (n = 5)	80 %
Maxillary 2nd premolar (n = 11)	91 %
Mandibular 2nd premolar (n = 9)	100 %
Maxillary canine (n = 2)	100 %
Maxillary incisor (n = 1)	100 %
Maxillary 1st premolar (n = 1)	100 %
Mandibular 1st premolar (n=1)	100 %

Table 5. The association between survival of the 36 randomly chosen transplanted teeth and the predictor variables*

	Number of teeth survived (%)	Hazard Ratio and 95 % CL	P-value
All teeth (n=36)	31 (86.1)		
The type of transplantation[a]			
Transalveolar (n=11)	9 (81.8)	1[b]	
Distant (n=25)	22 (88.0)	0.63 (0.11-3.78)	0.61
The donor tooth[c]			
Premolar (n=19)	18 (94.7)	1[b]	
Molar (n=15)	12 (80.0)	5.08 (0.52-49.43)	0.16
The maturity of the donor tooth			
E (n=5)	4 (80.0)	2.41 (0.25-23.32)	0.45
F (n=24)	21 (87.5)	1[b]	
F (n=24)	21 (87.5)	1[b]	
G (n=7)	6 (85.7)	1.36 (0.14-13.07)	0.79
The number of roots of the donor tooth			
Single-rooted (n=18)	16 (88.9)	1[b]	
Multi-rooted (n=18)	15 (83.3)	1.66 (0.28-9.93)	0.58
The recipient jaw			
Mandible (n=25)	21 (84.0)	2.03 (0.23-18.24)	0.53
Maxilla (n=11)	10 (90.9)	1[b]	
The need for extraoral storage of the donor tooth			
No (n=25)	23 (92.0)	1[b]	
Yes (n=11)	8 (72.7)	3.15 (0.53-18.88)	0.21
Institution experience[a]			
Early transplantations (n=18)	14 (77.8)	3.21 (0.35-29.56)	0.30
Late transplantations (n=18)	17 (94.4)	1[b]	
Continuation of root development[d]			
Yes (n=27)	26 (96.3)	1[b]	
No (n=8)	4 (50.0)	21.33 (2.12-214.98)	0.009

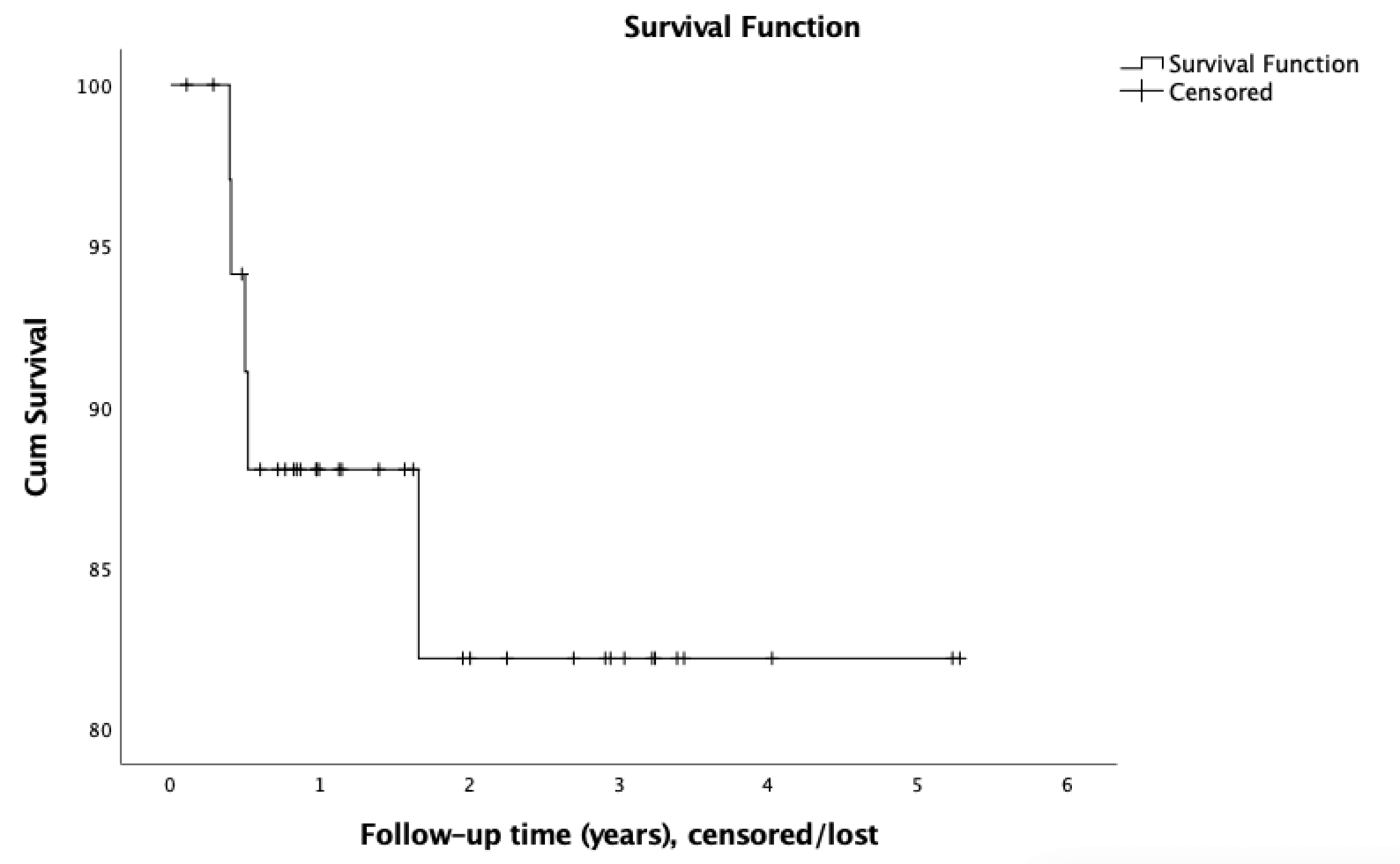
[a] Refer to the Patients and Methods section for the definitions of the study variables
[b] Reference level
[c] Canines (n=2) were excluded due to small sample size
[d] The teeth extracted due to malposition (n=1) were excluded from the analysis

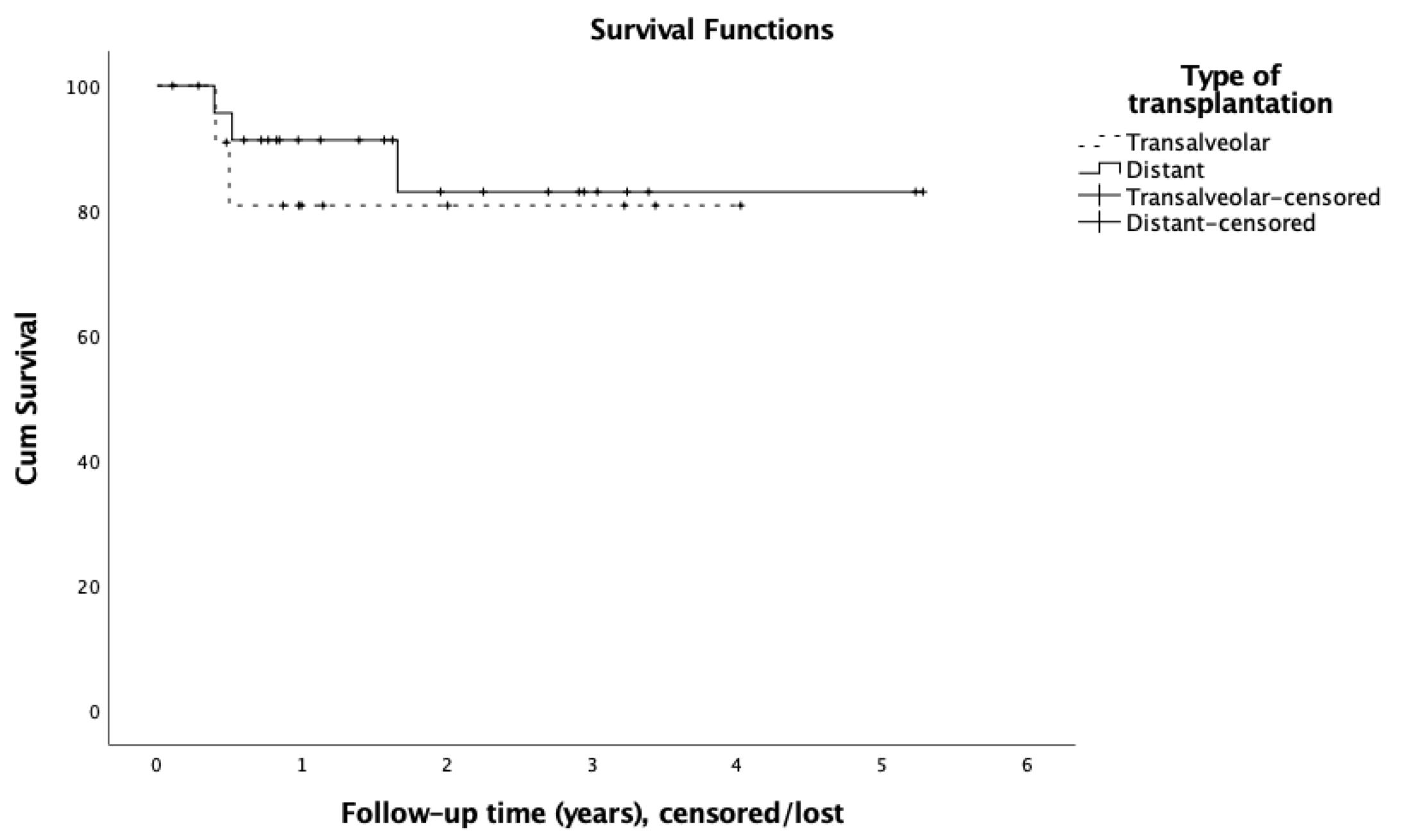
Figure 1. Kaplan-Meier survival curves: a.) overall survival b.) by the type of transplantation c.) by the type of the donor tooth d.) by the maturity of the donor tooth e.) by the number of roots of the donor tooth f.) by the recipient jaw g.) by the need of extra-oral storage time during surgery h.) by the continuation of root development during follow-up i.) by the institution experience

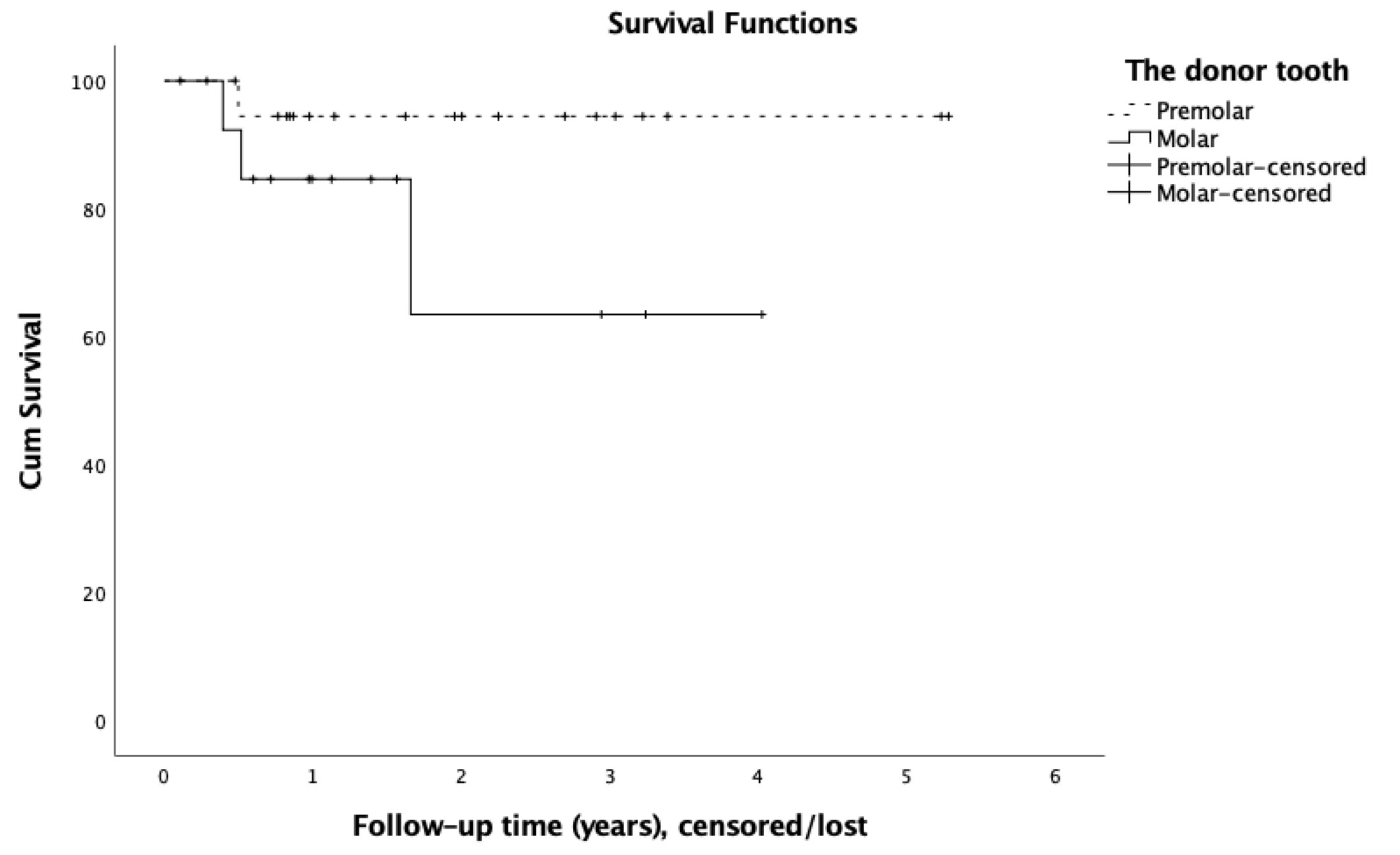
Figure 2a. The CBCT was taken preoperatively of the unerupted d. 34.
Figure 2b. D. 34 has been transplanted to replace d. 21. The CBCT was renewed 1 year 10 months postoperatively. The part of the root that was formed before the time of operation shows pulp obliteration, whereas the part formed during follow-up has a normal pulp chamber.

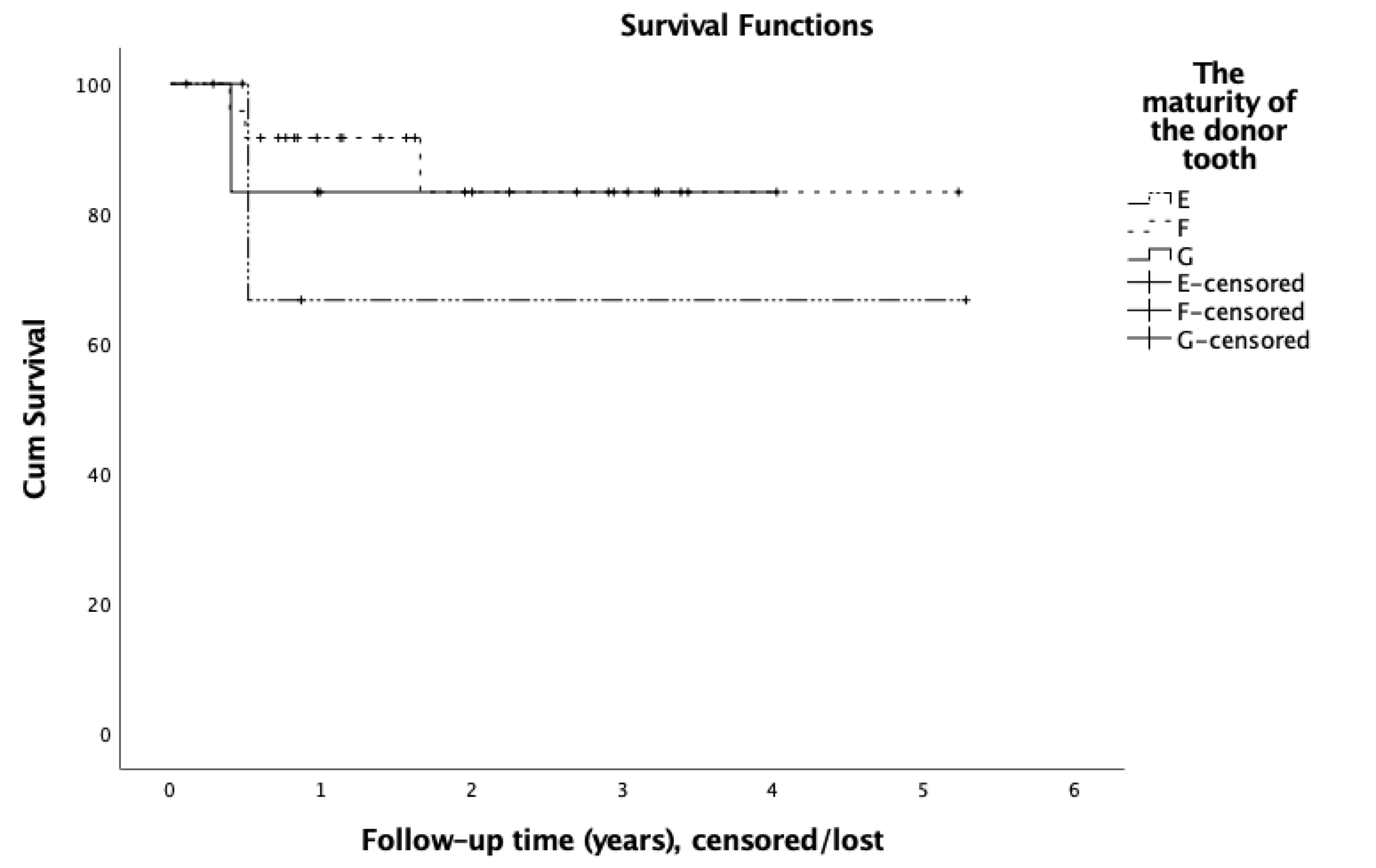
Figure 3a. D. 46 is in infra-occlusion and the decision is been made to transplant d. 47 at its place.
Figure3b. After almost 2 years of follow-up d. 47 is found to be in ankylosis and is not responding to orthodontic traction.

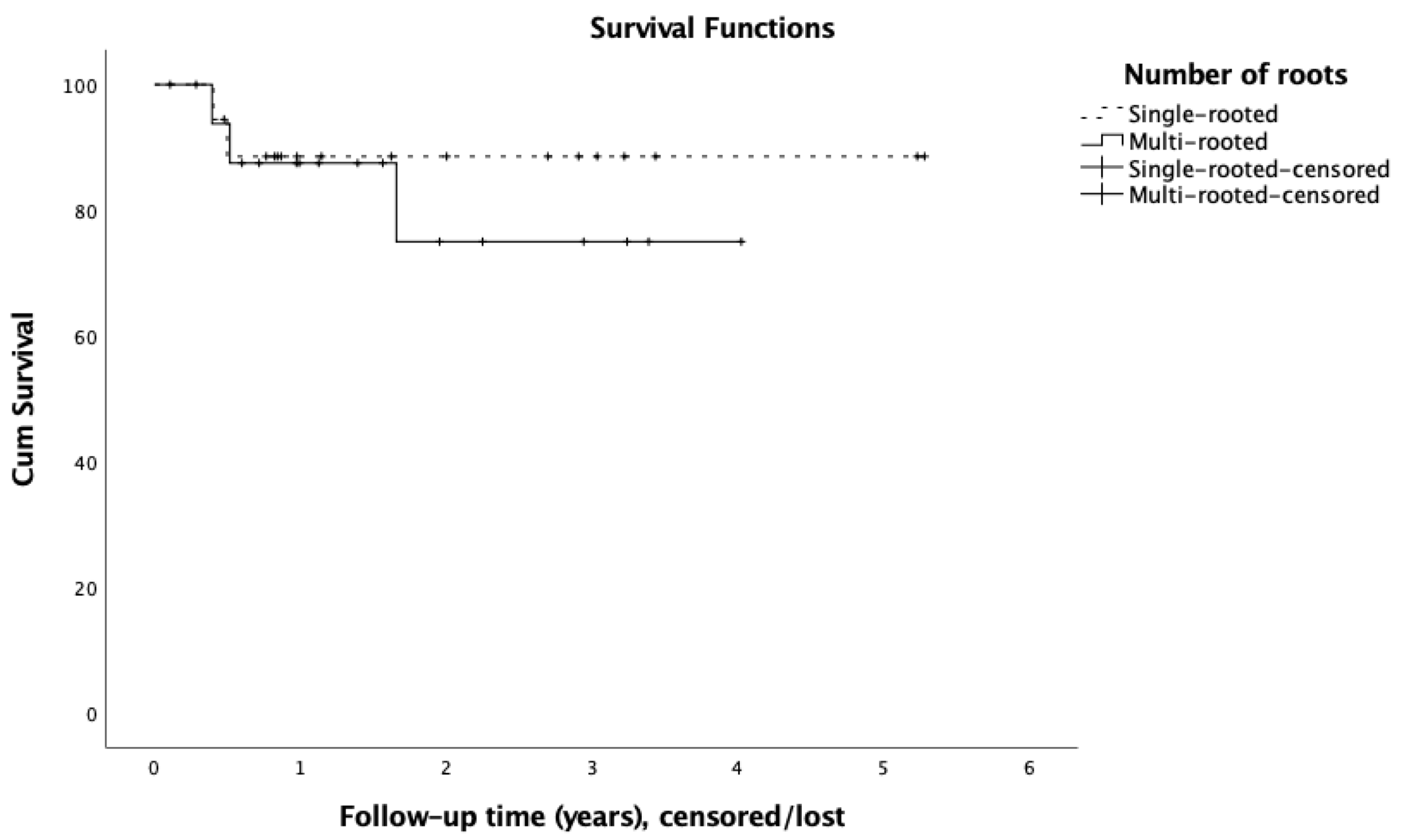
Figure 4a. Preoperative x-ray of a situation, were both maxillary canines are impacted horizontally.
Figure 4b. Clinical picture at the final follow-up visit.
Figure 4c. The x-ray 2 years postoperatively.

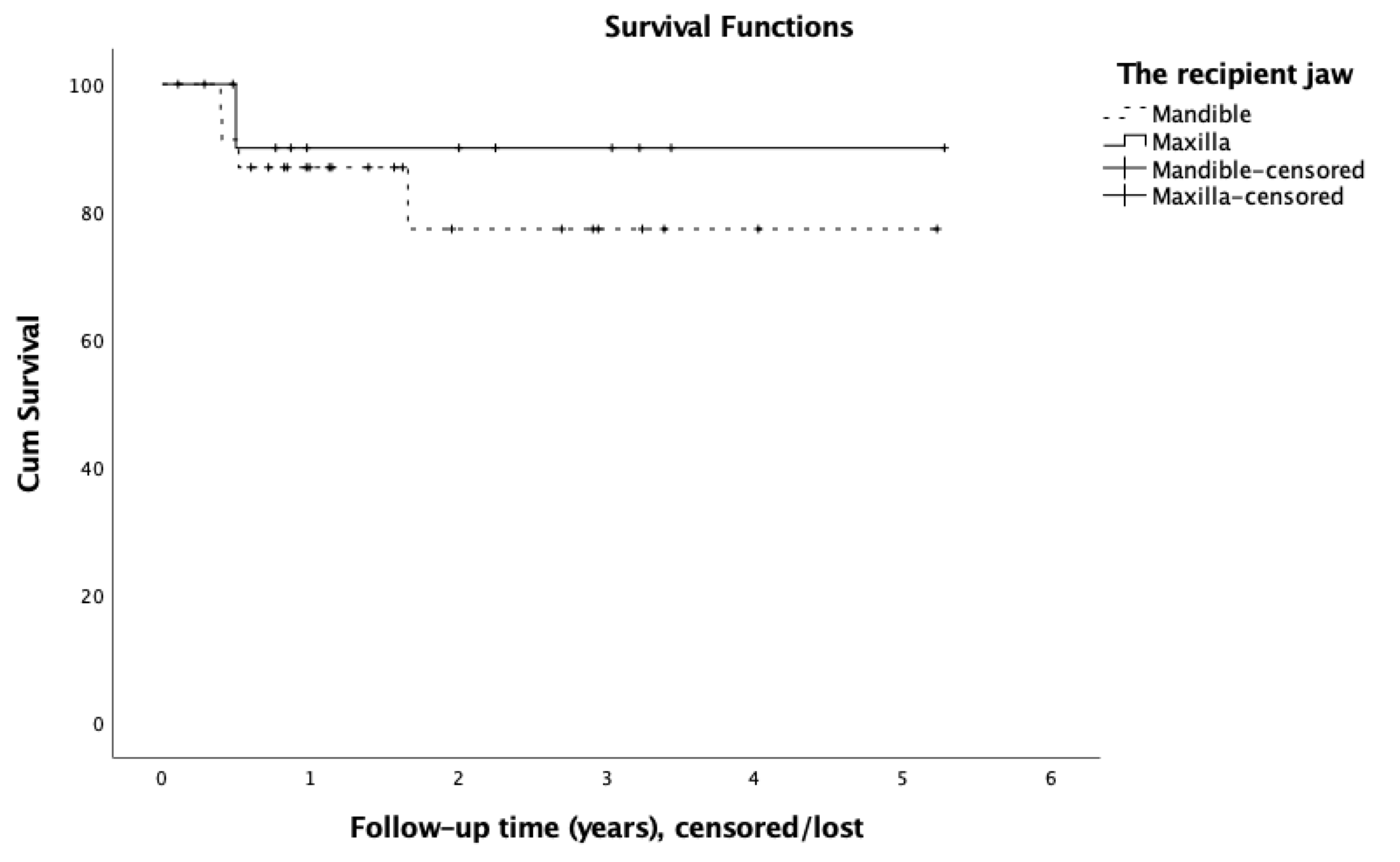

Survival Function
Survival Function
Censored
100
95
90
85
80
Cum Survival
0
1
2
3
4
5
6
Follow-up time (years), censored/lost

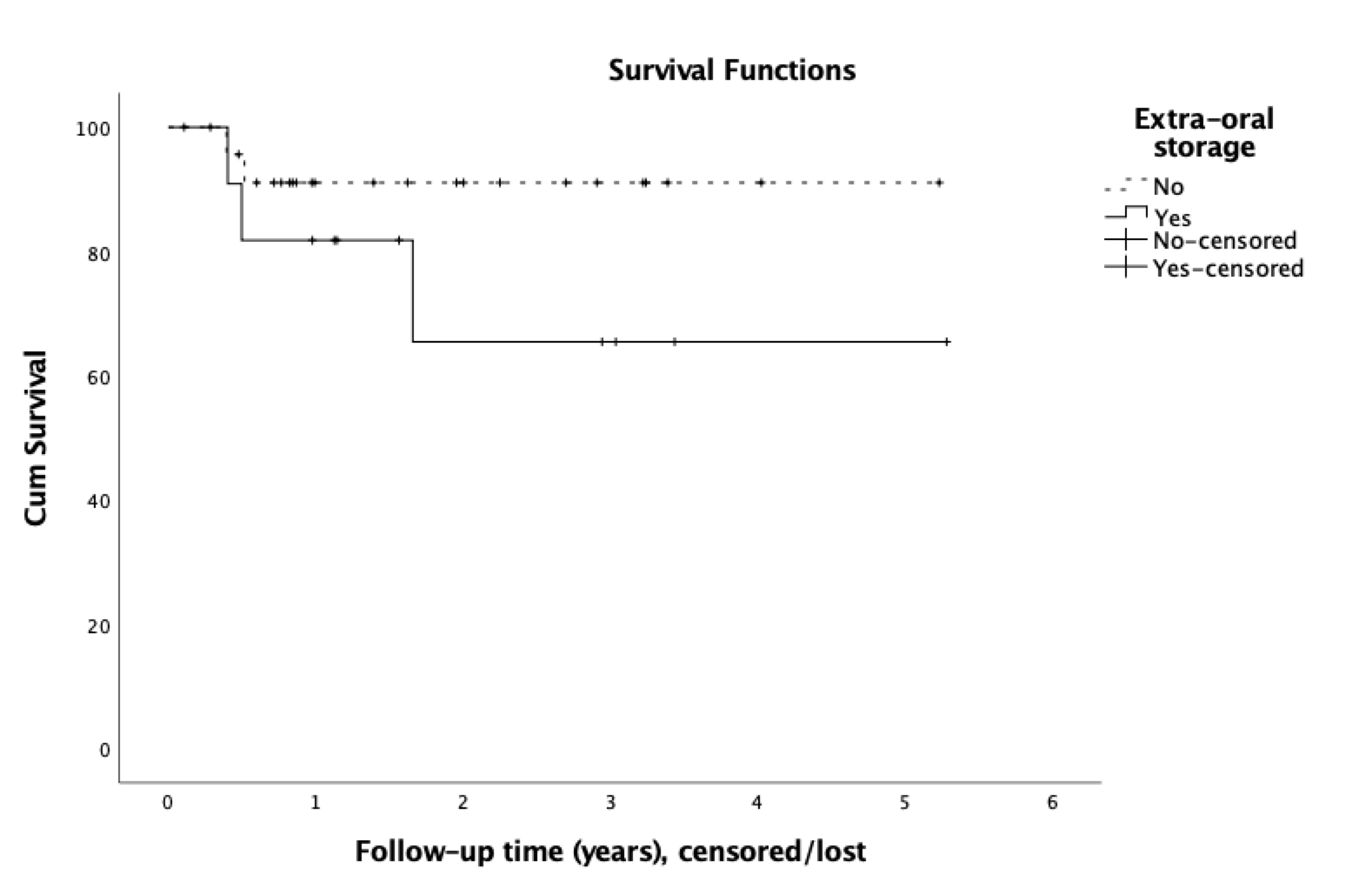

Survival Functions
Type of transplantation
Transalveolar
Distant
Transalveolar-censored
Distant-censored
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost

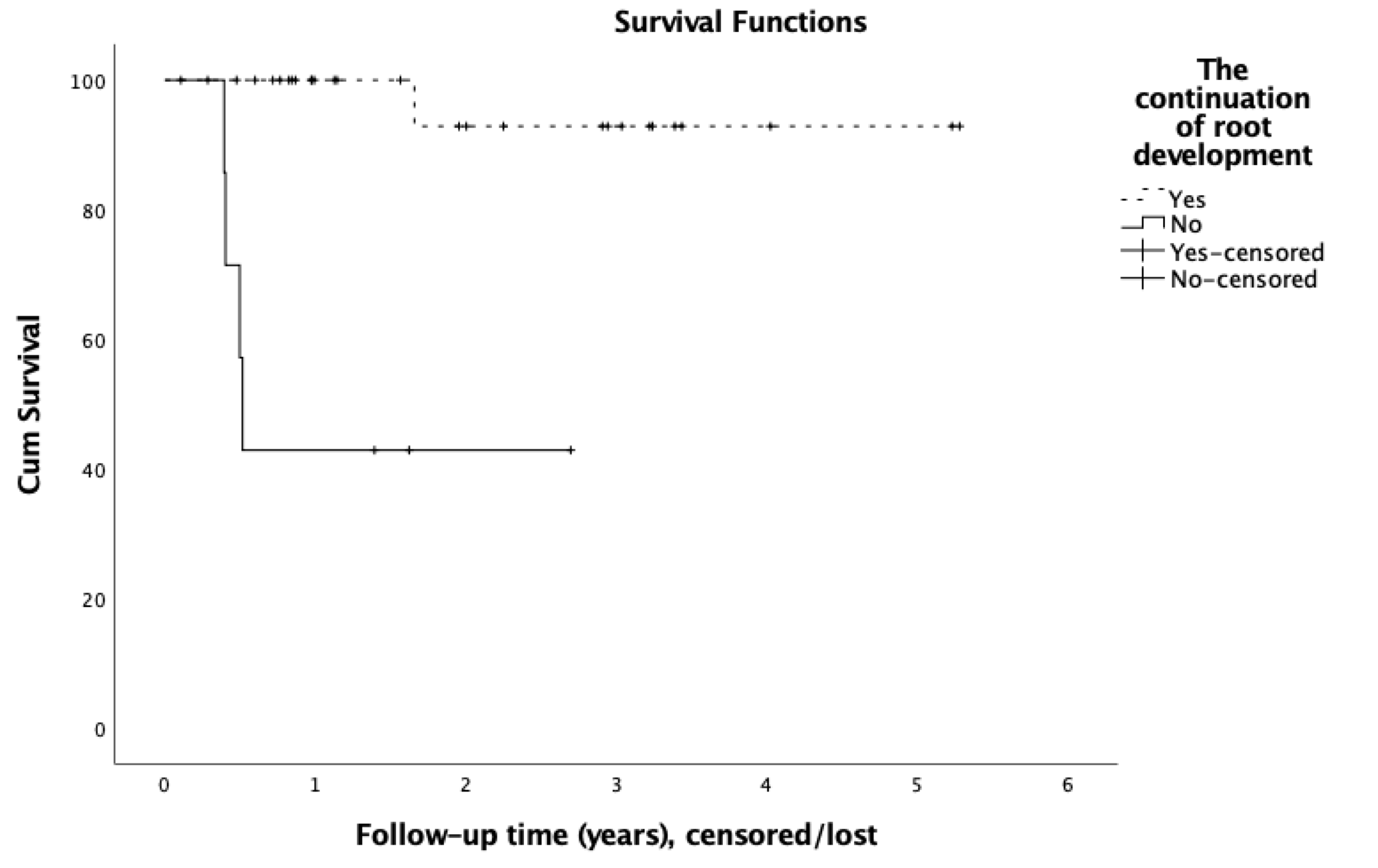

Survival Functions
The donor tooth
Premolar
Molar
Premolar-censored
Molar-censored
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost

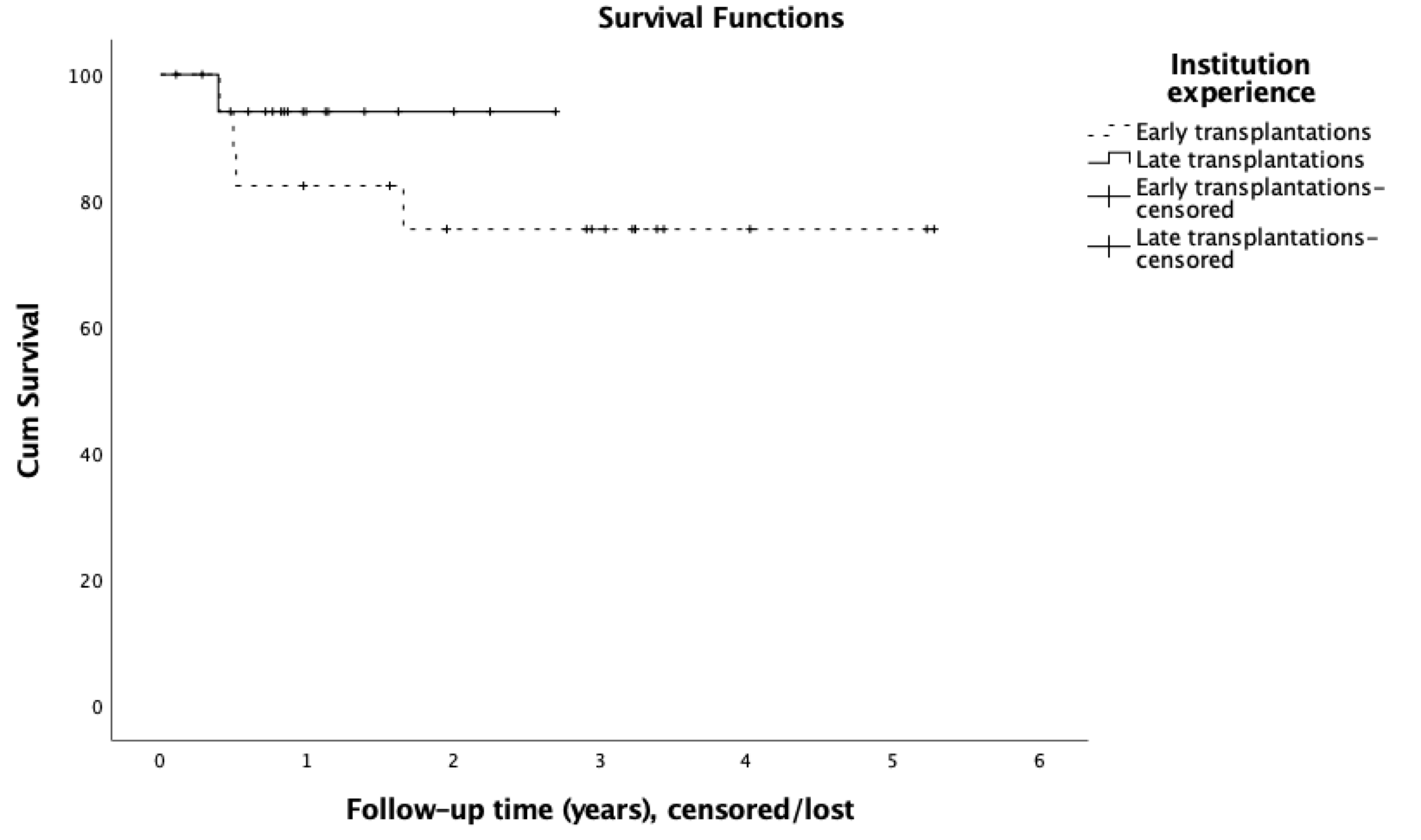

Survival Functions
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost
The maturity of the donor tooth
E
F
G
E-censored
F-censored
G-censored


Survival Functions
Number of roots
Single-rooted
Multi-rooted
Single-rooted-censored
Multi-rooted-censored
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost


Survival Functions
The recipient jaw
Mandible
Maxilla
Mandible-censored
Maxilla-censored
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost


Survival Functions
Extra-oral storage
No
Yes
No-censored
Yes-censored
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost


Survival Functions
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost
The continuation of root development
Yes
No
Yes-censored
No-censored


Survival Functions
Cum Survival
100
80
60
40
20
0
0
1
2
3
4
5
6
Follow-up time (years), censored/lost
Institution experience
Early transplantations
Late transplantations
Early transplantations-censored
Late transplantations-censored