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RESEARCH REPORT

IMP-SMART 002
in cooperation with Alpha-Bio Tec, Ltd.

Medical device	Alpha-Bio Tec MultiNeo implants
Site	Smile Dent Ltd., Szeged, Hungary
Principal investigator	Prof.Dr.József Piffkó, University of Szeged, Faculty of Medicine, Department of Oral and Maxillofacial Surgery
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Report prepared for	Alpha-Bio Tec, Ltd.

CONFIDENTIAL

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I. Introduction

This report summarizes the clinical experience with Alpha-Bio Tec's MultiNeO implants inserted in the first phase of IMP-SMART 002.[1] The second phase is a two-year follow-up in which the inserted implants are monitored in various aspects. This report summarizes data from the first year. Data collection was continuous from April 2019 to March 2020, when the study was suspended because of COVID-19 lockdown. Data collection could start again in July 2020 and is going on at the moment. The suspension because of the lockdown means that the project is 4 months late, so the original deadlines need to be postponed. The report is based on the data in the Excel tables attached and includes patient demographics, the distribution of the inserted implants (by size), Osstell stability data, mean probing depth, OHIP-14 quality of life data, bone levels, adverse events and implant loss.

II. Patient demographics and implants

During the first year of the study, we lost 10 patients due to non-compliance (dropout rate: 9.8%). These patients failed to return after getting their implants, and so we could not include them in the follow-up phase. This left us with altogether 93 patients with 190 implants. By the time of the preparation of this report, 79 patients (85%) with 170 implants (89%) completed their 1-year follow-up. The remaining 14 patients are coming back in the upcoming weeks, but we did not wish to delay this (already delayed) report, and we do believe that the data we have are sufficient for a valid interim report.
Of the 79 patients, 42 are females (53.2%) and 37 are males (46.8%). Their mean age is 44.77 (± 8.1) years. They are evenly distributed according to the applied surgical approach (freehand, pilot guide, partial guide, full guide). The patients' distribution across the surgical approaches is given in Table 1.

[1] Varga E, Jr., Antal M, Major L, Kiscsatari R, Braunitzer G, Piffko J. Guidance means accuracy: A randomized clinical trial on freehand versus guided dental implantation. Clin Oral Impl Res. 2020;31(5):417-30.

Table 1. Distribution of the patients across the surgical approaches.

	Frequency	Percent	Valid Percent	Cumulative Percent
Freehand	16	20.3	20.3	20.3
Full guide	22	27.8	27.8	48.1
Partial guide	20	25.3	25.3	73.4
Pilot guide	21	26.6	26.6	100.0
Total	79	100.0	100.0	

The majority of the patients (N=56, 70.9%) received one or two implants. The highest number of placed implants was 6 (in 3 cases). Frequency data are given in Table 2.

Table 2. The numbers of implants placed per case in the sample.

Number	In N cases	Percent	Valid Percent	Cumulative Percent
1	30	38.0	38.0	38.0
2	26	32.9	32.9	70.9
3	15	19.0	19.0	89.9
4	3	3.8	3.8	93.7
5	2	2.5	2.5	96.2
6	3	3.8	3.8	100.0
Total	79	100.0	100.0	

As for the size distribution of the implants, 15 sizes were placed (Table 3). 4.2*10 was the most frequently placed (N=34, 20%), while 3.2*10, 5*11.5 and 3.2*11.5 each were placed only once (0.6%). 135 of the 170 (79.4%) implants were of the following sizes: 3.5*10, 4.2*10, 3.5*11.5, 3.75*10, 4.2*11.5 and 3.75*11.5.

Table 3. Size distribution of the placed implants

	Frequency	Percent	Valid Percent	Cumulative Percent
5*8	2	1.2	1.2	1.2
4.2*8	7	4.1	4.1	5.3
3.2*10	1	0.6	0.6	5.9
3.5*10	15	8.8	8.8	14.7
3.5*13	8	4.7	4.7	19.4
3.75*8	2	1.2	1.2	20.6
4.2*10	34	20.0	20.0	40.6
4.2*13	4	2.4	2.4	42.9
5*11.5	1	0.6	0.6	43.5
3.2*11.5	1	0.6	0.6	44.1
3.5*11.5	10	5.9	5.9	50.0
3.75*10	28	16.5	16.5	66.5
3.75*13	9	5.3	5.3	71.8
4.2*11.5	18	10.6	10.6	82.4
3.75*11.5	30	17.6	17.6	100.0
Total	170	100.0	100.0	

III. Osstell stability (ISQ)

This was measured 1 to 3 weeks after the end of the implant treatment, at the first prosthetic treatment visit (which is the first visit of the follow-up). Thus, these values are best considered as the initial stability for prosthetic treatment. Stability was measured as per the manufacturer's instructions, in two positions, then the average of the values measured in the two positions was used for the analyses (i.e. the stability of one implant was characterized by one stability value). The mean stability of implants was 73.28 (± 8.75). According to the reference values of Osstell, this is high stability (>70). A linear regression analysis was conducted to determine if the position of any given implant or the technique of insertion (surgical approach) had a significant effect on stability, but no significant effect was found. It seems that the stability of implants was invariably excellent and fit for the prosthetic treatment.

IV. Probing depth

Periodontal probing depth is a measure of the health of periodontal (in this case: peri-implant) tissues. It is measured in six standard positions around each implant-superstructure complex and an average is calculated which can be used for the analyses. In this study, probing depth is measured from the 5th (initial implant+superstructure values) through the 9th (24-month follow-up) visits. For this report, we could calculate with values from the 5th, 6th and 7th visits.
As shown in Table 4., probing depths became progressively shallower during the observation period, indicating dynamic healing and remodeling of the peri-implant soft tissues

Table 4. Mean probing depths in the entire population at the different visits

Visit	Mean (mm)	N	Std. Deviation
5th	1.711	170	0.5134
6th	1.608	170	0.4395
7th	1.483	170	0.4157

A linear regression model was built, in which probing depth was the dependent variable and implant position, surgical technique and time were entered as determinants. Only time proved to have a significant effect (β= -0.198, t= -4.471, p< 0.000). This means that the tissues around all implants healed and remodeled homogeneously well.

V. OHIP-14 QoL

This is the short, 14-item version of the Oral Health Impact Profile questionnaire, ideal for chairside use. The patients involved in this study fill in this questionnaire at visits 1, 5, 6, 7, 8 and 9. Results from visits 1 and 5 characterize the postoperative period, while visits 6 through 9 give us a picture of the patients' perceived quality of life while already wearing their prosthetics. Figure 1 shows the questionnaire.

OHIP-14					
In the last six months	Never	Hardly ever	Occasionally	Fairly often	Very often
1) Have you had trouble pronouncing any words because of problems with your teeth, mouth or dentures?					
2) Have you felt that your sense of taste has worsened because of problems with your teeth, mouth or dentures?					
3) Have you had painful aching in your mouth?					
4) Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures?					
5) Have you been worried by dental problems?					
6) Have you felt tense because of problems with your teeth, mouth or dentures?					
7) Has your diet been unsatisfactory because of problems with your teeth, mouth or dentures?					
8) Have you had to interrupt meals because of problems with your teeth, mouth or dentures?					
9) Have you found it difficult to relax because of problems with your teeth, mouth or dentures?					
10) Have you been a bit embarrassed because of problems with your teeth, mouth or dentures?					
11) Have you been a bit irritable with other people because of problems with your teeth, mouth or dentures?					
12) Have you had difficulty doing your usual jobs because of problems with your teeth, mouth or dentures?					
13) Have you felt that life in general was less satisfying because of problems with your teeth, mouth or dentures?					
14) Have you been totally unable to function because of problems with your teeth, mouth or dentures?					

Figure 1. The OHIP-14 questionnaire. Please note that the participants of the study were administered the validated Hungarian version of the instrument.

The instrument examines 14 possible oral health-related problems in 7 domains (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, handicap). As seen in Figure 1, the 14 items are scored 0 to 4, where 0 means never and 4 means very often. This way, the higher the score, the higher the discomfort (poorer quality of life in the given aspect). A summed value is usually calculated to characterize oral health-related quality of life in general. The maximum possible score for a given person, following from what has been said above, is 56 (complete dissatisfaction), the minimum is 0 (complete satisfaction).
We characterized the study population, not single persons. This we did in two ways: First, we calculated the summed OHIP-14 value for each person, and we calculated averages for each visit. Second, we analyzed how many points a given item received at each visit from all patients (this way it was possible to tell how serious any given problem was in the entire population at a given point of time).
As for the first approach, the results are given in Table 5.

Table 5. General (summed) quality of life at each visit in the studied period.

Visit	Mean	N	Std. Deviation
1st	4.73	90	6.802
5th	4.38	88	7.127
6th	1.29	80	3.086
7th	0.85	78	2.193

Linear regression analysis was conducted with summed OHIP-14 score as the dependent variable and surgical technique and time as factors. The way surgery had been done had no significant effect, while the effect of time was significant (β= -0.252, t= -4.763, p< 0.000). The values in Table 5 show that in the postoperative period mild discomfort was reported (between 4 and 5 as compared to the maximal 56). This significantly improved by the 6th month with the implant and prosthesis, and by the 12th month it became negligible.
As for the summed scores for the individual items, these are shown in Table 6 and Figure 2.

Table 6. Summed scores for each of the 14 OHIP-14 items broken down to visits

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1st visit	22	9	39	60	68	46	28	19	37	49	11	17	17	4
5th visit	23	10	42	60	45	38	25	14	37	39	11	18	19	4
6th visit	7	6	13	23	11	11	10	5	8	6	1	0	2	0
7th visit	5	2	6	16	5	5	8	3	6	6	2	2	0	0

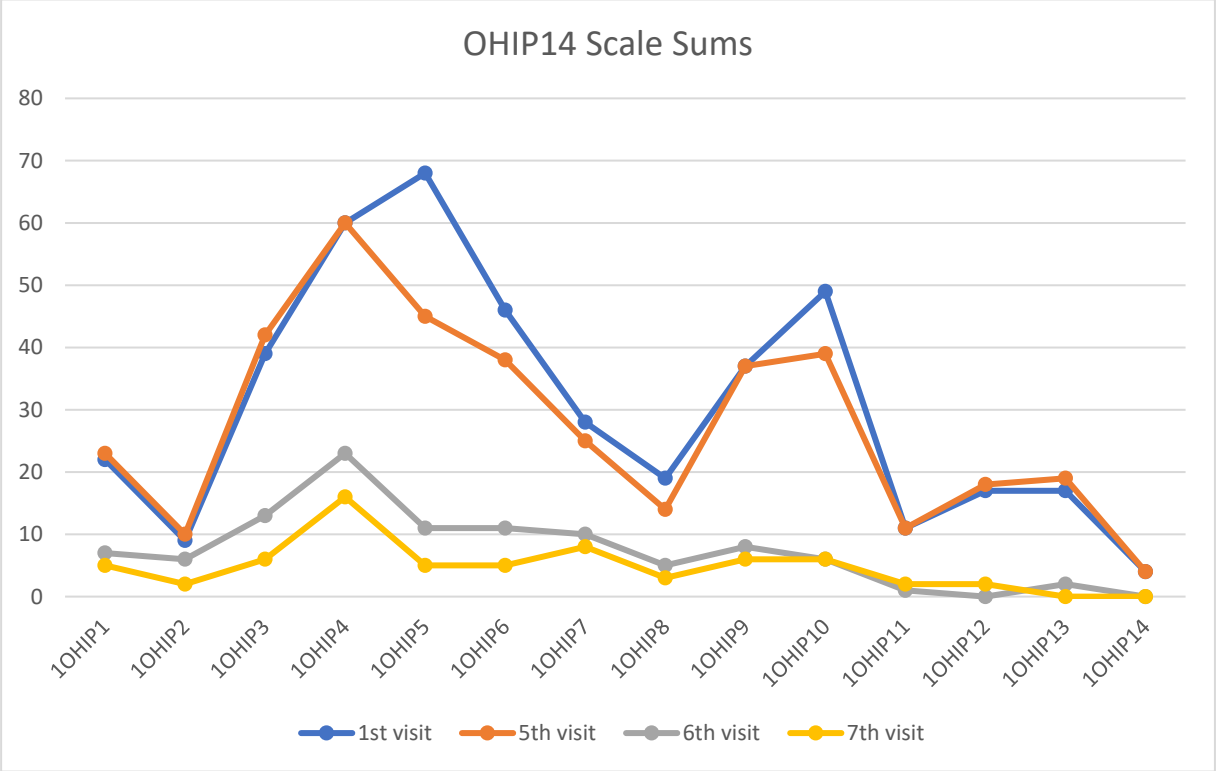

Figure 2. A graphical illustration of itemized quality of life in the examined period.

The table and the figure show that in the postoperative period, the patients had the most problems with uncomfortable eating, well-being in general and socialization. Of these, uncomfortable eating and problems with socialization may be considered as specific to the oral intervention, general well-being is affected by any kind of surgery. By the 1-year follow-up, these problems had been gone, the only aspect that seems to remain somewhat problematic is comfortable eating. This is probably because the patients have not completely got used to their prosthetics yet. None of these findings

are specifically related to the implants, these findings reflect the normal postoperative dynamics.

VI. Bone levels

Standardized bitewing x-rays are taken in each implanted position on the 1st (with healing abutment) 4th (right after the placement of the superstructure) and 6th-9th visits (6-24 months' follow-ups), per protocol.

The images are analyzed in EZDent (Vatech, Korea). Bone levels are measured mesially and distally. For this, the software needs to be calibrated in each case. Calibration is performed using the coronal diameter of the implant as a known value (Figure 3).

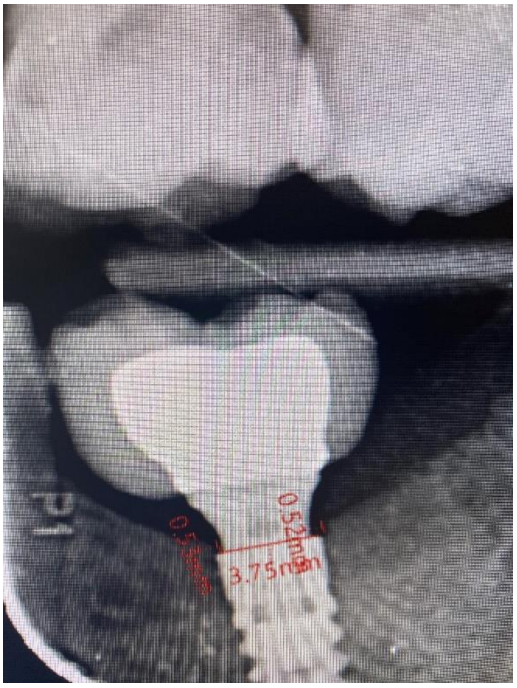

Figure 3. Calibration and measurement in EZDent. For calibration, the coronal diameter of the implant (here 3.75 mm) is used.

Bone level, for the purposes of this study, is calculated as the distance between the coronal plane of the implant and the level of the crestal bone in millimeters. Bone level is positive if the level of the crestal bone is above the coronal plane and negative if the level of the crestal bone is below the coronal plane.

Descriptive statistics for visits 1,4, 6 ad 7 are given in Table 7.

Table 7. Bone levels. The values are given in millimeters. M: mesial, D: distal. The numbers in the heading indicate the number of the visit.

	M1	**M4**	**M6**	**M7**
Mean	0.2560	0.2479	0.2472	0.30023
N	189	187	183	182
Std. Deviation	0.98949	0.88643	0.80807	0.824292
	D1	**D4**	**D6**	**D7**
Mean	0.0095	0.0375	-0.24856	0.0827
N	189	187	183	182
Std. Deviation	0.85023	0.92547	4.069760	0.71656

Linear regression analysis did not verify a significant effect of either surgical approach or implanted position for any of the visits.

Repeated measures ANOVA was also conducted to find out if the bone levels changed significantly in time. No significant effect was found.

The general conclusion is that in the analyzed observation period, only minimal bone level changes occurred. The reason is possibly that, from an implant success and survival point of view, very little time has passed since the implants were inserted.

VII. Adverse events, implant loss

No adverse events or serious adverse events have been reported in the observation period, implant-related or otherwise. According to the results of this study so far, the implants are safe, and they are characterized by a homogeneously good, complication-free healing profile.

Implant loss itself, as a known and calculated complication of implant placement about which the patients are forewarned, is not treated as an adverse event under this protocol.

Of the 207 implants originally inserted in the first phase of the study, 2 have been lost so far, adding up to an implant loss ratio of 0.97% in two years. Of these two cases, one happened in phase one, it was investigated, and it could most probably be traced back to patient non-compliance (the patient smoked after the surgery against the warning). The other one happened in the second phase. In that case, peri-implant inflammation of unknown etiology developed, which led to the loss of the implant. The patient was treated according to the protocols for such cases and healed without sequelae. The incident had nothing to do with the inserted implant itself. The patient is still in the study with his other implant.

Attachments

1) **ABT_COLLECTIVE_TABLE_20201024.xlsx:** the raw data table used to collect study data; tables for data analysis derive from this table.
2) **Demogr_20201024.xlsx:** table for the analysis of demographic data.
3) **Osstell_20201024.xlsx:** table for the analysis of implant stability data.
4) **Probing_20201024_MEAN.xlsx:** table for the analysis of mean probing depth.
5) **Probing_20201024_POSITIONS.xlsx:** detailed table for the analysis of probing depth with information on the individual measurement points.
6) **OHIP14_20201024.xlsx:** table for the analysis of quality of life.
7) **BONELEVEL_20201105.xlsx:** bone level data
8) **REPORT_SUMMARY_170implants_20201024.xlsx:** a summary of the results in table format