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# Accuracy of computer guided implant dentistry: a permutation testing approach

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The aim of this paper was to analyze the accuracy of computer-guided template-based implant dentistry by comparing implant position in the virtual project and that actual reached in the bones. For this purpose we considered a study involving 17 healthy patients subjected to an implant surgical session with the insertion of implants with an external connection. Data from this study do not follow a well defined sampling procedure, and (multivariate) data do not follow a (multivariate) normal distribution, thus traditional parametric approaches were not recommend. Analysis with a nonparametric procedure based on permutation tests and nonparametric combination methodology revealed that significant discrepancies exist between the planned and actual implant position.

**keywords:** computer-guided implant dentistry, permutation tests, nonparametric combination, multivariate analysis

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# 1 Introduction

In dentistry there is a growing interest in new treatments with a reduced number of implants, designed to support fixed prostheses with high aesthetic and functional results. The standard protocols for implant surgery, are often based on a diagnostic phase entrusted to radiographic examination and by a clinical examination of the edentulous maxillary bone sites. Two dimensional radiographic examination does not provide an accurate analysis of the bone structures and, consequently, they do not allow to acquire sufficient data for the functional and esthetic design of the implant-prosthetic complex. An accurate before intervention analysis of the patient's stomatognathic apparatus can be very useful. A new method for the flapless positioning of endosseous implants in the edentulous patient with the aid of surgical mucosal support and computer guided techniques, based on diagnostic 3D imaging, allows to measure the bone volume available for implant surgery, its quality and possible anatomical variations. Thanks to the matching of images of prostheses acquired through optical scanners and three-dimensional radiological images it is possible to study the virtual prosthetic rehabilitations of the patients. Proper virtual planning allows to accurately perform mini-invasive surgery and to use pre-established prostheses made with CAD/CAM methods for an immediate and faithful functionalization of virtual planning. The scientific literature shows that the flapless surgical approach for implant placement has a long-term survival rate similar to the open-flap conventional surgical techniques (Jané-Salas et al., 2018). However, there are few studies that analyze the accuracy and precision of CAD/CAM surgical guides dental implants inserted with flapless approach and mucosal support.

In the present paper we aim at evaluating the accuracy of the clinical results of dental implant positioned in total edentulous patients with CAD/CAM surgical guides produced after 3D software planning. For this purpose we considered data from a study involving 17 healthy patients - not randomly - selected to receive immediate implant-prosthetic rehabilitation of the maxilla and jowl. Through a specific software for the evaluation of three-dimensional deviations (Geomagic Studio, Geomagic - USA) it is possible to detect, in the three spatial coordinates, the discrepancies between the project position and the clinical position actually reached, according to a standard procedure already validated and published (Rocci et al., 2003). As we will see in next section, data available for this study do not allow to consider traditional parametric technics because collecting data did not follow a well-designed sampling procedure and distributional assumptions are difficult to justify. In order to properly analyze the discrepancies between the project position and the actual position, we opted for nonparametric technics in the field of permutation tests. It is known that in many circumstances permutation tests perform better than parametric tests by providing a valid statistical test with much weaker assumptions (Arboretti et al., 2018, 2017; Pesarin et al., 2016).

The paper is structured as follows. In the next section we describe data and formalize the problem. Then we introduce and motivate the methodology adopted to analyze data and finally we discuss the results obtained applying the proposed procedure.

## 2 Material and Methods

For the study 17 patients were - not randomly - selected, 8 males, 9 females of average age 58 years. After clinical examination all patients showed good general health, with total maxillary edentulism and the need to receive a full-arch immediate implant-prosthetic rehabilitation. The exclusion criteria used were:

- patients undergoing chemotherapy and / or radiotherapy
- cardiopathic patients
- pregnant women
- patients on bisphosphonate therapy
- patients with blood criasis problems
- patients with uncompensated diabetes.

Thus subjects are presumed to be homogeneous with respect to some important conditions such as age and health. The patient is then subjected to an implant surgical session, with the insertion of implants with an external connection. Immediately after there is the load of the prosthetic device. Six months after loading, a control 3D cone beam computed tomography (CBCT) radiographic examination was detected to evaluate the deviations between the virtual project and the clinical position of the fixtures, guided by the surgical template.

**Note that each patient has more than one implant (about** 3.94 **implant per patient in average). Table 1 shows the frequency distribution of number of implants for patient.**

Table 1: Frequency distribution of implants per patient.

| $Numberofimplants$ | $Frequency$ |
|---|---|
| 2 | 1 |
| 3 | 1 |
| 4 | 9 |
| 5 | 1 |
| 6 | 5 |

For a total of $n = 76$ different implants, differences for three spatial coordinates ($X$, $Y$, $Z$) between the virtual planning implant position and the clinical actual position in the bone were observed both at the apex and at the entry point of each implant.

**From a statistical point of view, three-dimensional data on different implants can be (approximately) assumed as conditionally independent within each unit. Furthermore, it is generally difficult to exclude in principle a so-called "block effect" for data regarding one unit, in the sense that related data are generally more similar while considered within units (in terms of means, dispersions, correlations, etc.) than data between different units. So, since units can be assumed to behave independently, with respect to different units data can be assumed as independent but not identically distributed. Of course, this could become a big difficulty for standard parametric analyses, such as Hotelling $T^2$. Fortunately, it is not a difficulty for the permutation analysis with multivariate paired data. The most important limitation for permutation analyses is that the resulting tests, more than finite-sample optimal, can simply be set up as admissible (a test is said admissible when there does not exist any other test which is uniformly more powerful than it), and so they are at least unbiased and consistent, only sometimes they can be asymptotically optimal.** Table 1 show an extract of the real dataset.

Table 2: Extract of implant data

| $i$ | $X_{apex}$ | $Y_{apex}$ | $Z_{apex}$ | $X_{entry\ point}$ | $Y_{entry\ point}$ | $Z_{entry\ point}$ |
|---|---|---|---|---|---|---|
| 1 | 0.437 | −0.301 | −0.315 | 0.079 | −0.117 | −0.375 |
| 2 | 0.845 | −0.845 | 0.138 | 0.255 | −0.132 | −0.071 |
| ... | ... | ... | ... | ... | ... | ... |
| 67 | 0.250 | 0.340 | 0.070 | 0.390 | 0.480 | 0.050 |

Remind that data $\mathbf{D}_j = (X_j, Y_j, Z_j), j \in \{\text{apex, entry point}\}$ are differences given by underlying paired observations *pre* and *post*-surgery. In fact we may consider observable variables as $\mathbf{D}_{ij} = (X_{ij(post)} - X_{ij(pre)}, Y_{ij(post)} - Y_{ij(pre)}, Z_{ij(post)} - Z_{ij(pre)})$, $i = 1, \ldots, n$ and $j \in \{\text{apex, entry point}\}$. Formalizing we are interested in testing the following system of hypotheses

$$\begin{cases} H_0 : P_{ij,post} = P_{ij,pre}\ \forall j \text{ AND } \forall i \\ H_1 : P_{ij,post} \neq P_{ij,pre} \text{ for at least one } j \text{ OR one } i \end{cases} \tag{1}$$

where $P_{j,post}$ and $P_{j,pre}$ are the multivariate distributions of responses *post* and *pre*-surgery respectively, and $j \in \{apex, entry\ point\}$. If we assume in both groups the multivariate errors of positioning to be normally distributed, an unconditional solution is represented by the parametric paired Hotelling $T^2$ test. However, this distributional assumption may not be true, and departures from this assumption can potentially lead to incorrect conclusions. Furthermore, the $T^2$ test fails to provide an easily implemented one-sided (directional) hypothesis test (Blair et al., 1994) and it does not allow to inves-

tigate on partial aspects involved (marginal coordinates), giving only a global results. It is also worth to underline that patients enrolled in this study were not randomly selected that is on of the assumption regarding the validity of Hotelling $T^2$ test.

### 2.1 The permutation testing approach

Permutation tests are conditional inferential procedures in which conditioning is with respect to the sub-space associated with the set of sufficient statistics in the null hypothesis for all nuisance entities, including the underlying known or unknown distribution (Pesarin and Salmaso, 2010). A sufficient condition for properly applying permutation tests is that the null hypothesis implies that observed data are exchangeable **between times within each implant**. When exchangeability may be assumed in $H_0$, the similarity and unbiasedness property allow for a kind of weak extension of conditional to unconditional inferences, irrespective of the underlying population distribution and the way sampling data are collected. Therefore, this weak extension may be made for any sampling data, even if they are not collected by well-designed sampling procedure (Pesarin, 2002). Due to their flexibility permutation tests are very popular in neuroimaging, because they do not require assumptions and/or approximations that may be difficult to meet in real data.

In what follow we describe the permutation procedure we adopted to analyze the implant data in the present study.

In order to solve the global hypothesis testing in (1), the idea is to face separately - but simultaneously - the two (multivariate) testing problems (one for each $j \in \{$ apex, entry point$\}$) and then combining them through the nonparametric combination (NPC) methodology (Pesarin and Salmaso, 2010).

Let us consider the following vectors of test statistics $\mathbf{T}_j = (T_{X_j} = \sum_i X_{ij}, T_{Y_j} = \sum_i Y_{ij}, T_{Z_j} = \sum_i Z_{ij})$, $j \in \{$apex, *entry point*$\}$. Note that $H_0$ implies that the observed values of each unit are randomly assigned to the two occasions *post* and *pre*-surgery. In other words, the sign of each difference is considered as if it were randomly assigned with probability 1/2. Under the assumption that the null hypothesis is true, we can find the conditional multivariate distribution of $\mathbf{T}_j$, i.e. $F_{\mathbf{T}_j}(t|\mathbf{D}_j)$, by considering the random attribution in all possible ways of the plus or minus sign to each difference with equal probability. All observed unit vectors must be processed in order to maintain underlying dependence relations among the variables.

In the case of our example, the cardinality of the permutation sample space (i.e. $2^{67}$) is too large to enumerate all its points. We can inspect the permutation sample space by a random sample from it with a *Conditional Monte Carlo* (CMC) procedure.
Essentially the CMC permutation procedure is reached by the following steps. For $j \in \{$*apex*, *entry point*$\}$:

1. Compute on the given data set of differences $\mathbf{D}_j = (X_j, Y_j, Z_j)$, the vector of the observed test statistics $\mathbf{T}_j^O = \mathbf{T}(\mathbf{D}_j) = (T_{X_j}, T_{Y_j}, T_{Z_j})$:

2. For each of the $n$ differences in $\mathbf{D}_j$, consider a random attribution of signs, $S_i^*$ **that is the same on $i^{th}$ implant for all (within implant) concerned differences:**

$X^*_{ij} = X_{ij} \cdot S^*_i, Y^*_{ij} = Y_{ij} \cdot S^*_i, Z^*_{ij} = Z_{ij} \cdot S^*_i, i = 1, \ldots, n, j \in \{\textbf{\textit{apex}}, \textbf{\textit{entry point}}\}$ obtaining a permuted data set $\mathbf{D}^*_j = (X^*_j, Y^*_j, Z^*_j)$.

3. Compute the vector of test statistics on the permuted data set $\mathbf{T}^*_j = \mathbf{T}(\mathbf{D}^*_j) = (T_{X^*_j}, T_{Y^*_j}, T_{Z^*_j})$.

4. Independently repeat steps $2-3$, a number $B$ of times obtaining an estimate of the null permutation distribution of $\mathbf{T}_j$: $\hat{F}_{\mathbf{T}_j}(t|\mathbf{D}_j) = (\mathbf{T}^{*1}_j, \ldots, \mathbf{T}^{*B}_j)$.

5. On $\hat{F}_{\mathbf{T}_j}(t|\mathbf{D}_j)$ estimate the vector of p-values like statistics as: $\mathbf{p}_j = \frac{\sum_{b=1}^{B} I(\mathbf{T}^{*b}_j \geq \mathbf{T}^{O}_j)}{B} = (p_{X_j}, p_{Y_j}, p_{Z_j})$ and its empirical distribution $\mathbf{p}^{*r}_j = \frac{\sum_{b=1}^{B} I(\mathbf{T}^{*b}_j \geq \mathbf{T}^{*r}_j)}{B} = (p_{X^{*r}_j}, p_{Y^{*r}_j}, p_{Z^{*r}_j})$, $r = 1, \ldots, B$.

At this point we have a p-value-statistic for each spatial coordinate both for apex and entry point. In order to obtain a multivariate result, let us introduce the method of nonparametric combination (NPC) of a finite number of dependent tests. In general, starting from $K$ partial aspects, the NPC in one second-order test $T'' = \Psi(p_1, \ldots, p_K)$ is achieved by a continuous, non- increasing, univariate, measurable, and non-degenerate real function $\Psi : (0,1)^K \to R^1$.
Combining functions $\Psi$ mostly used in practice are:
the *Fisher omnibus* combining function defined as $\Psi_F = -2 \cdot \sum_{k=1}^{K} (\log p_k)$;
the *Liptak* combining function defined as $\Psi_L = \sum_{k=1}^{K} \Phi^{-1}(1 - p_k)$;
the *Tippett* combining function defined as $\Psi_T = \max_{k=1}^{K} (1 - p_k)$.

For details about assumptions on partial tests and on desirable properties of combining functions we refer to Pesarin and Salmaso (2010).
Thus in our case:

6. compute the combined observed value of the second-order test as: $T''^{O}_j = \Psi(p_{X_j}, p_{Y_j}, p_{Z_j})$ and the r-th combined value of the vector statistics as $T''^{*r}_j = \Psi(p_{X^{*r}_j}, p_{Y^{*r}_j}, p_{Z^{*r}_j}), r = 1, \ldots, B$.

7. based on $T''^{*}_j = (T''^{*1}_j, \ldots, T''^{*B}_j)$ distribution, compute the p-value-statistic of the combined test as $p''_j = \frac{\sum_{b=1}^{B} I(T''^{*b}_j \geq T''^{O}_j)}{B}$ and its empirical distribution $p''^{*r}_j = \frac{\sum_{b=1}^{B} I(T''^{*b}_j \geq T''^{*r}_j)}{B}$, $r = 1, \ldots, B$.

At this point we reduced the dimensionality of the problem, obtaining a multivariate p-value-statistic both for apex and entry point. In order to obtain a global result for null hypothesis $H_0$ (1) we can further combine the results along $j \in \{\text{apex, entry point}\}$. Thus:

8. compute the combined observed value of the third-order test as: $T'''^{O} = \Psi(p''_{apex}, p''_{entry\ point})$ and the r-th combined value of the vector statistics as $T'''^{*r} = \Psi(p''^{*r}_{apex}, p''^{*r}_{entry\ point}), r = 1, \ldots, B$.

9. based on $T'''^{*} = (T_j'''^{*1}, \ldots, T_j'''^{*B})$ distribution, compute the p-value-statistic of the combined test as $p''' = \frac{\sum_{b=1}^{B} I(T'''^{*b} \geq T'''^{O})}{B}$.
10. if $p''' \leq \alpha$ reject the global null hypothesis.

where $\alpha$ is the fixed significance level. It is important to underline that in order to properly apply these last steps, permutations performed at point 2 must be the same for apex and entry points in order to preserve the relation among the variables related to the same statistical units.

# 3 Data Analysis

In this section we analyze implant data using the permutation procedure described in Section 2.1. We performed permutation tests based on $B = 10000$ permutations of signs and we considered $\Psi_F$ as combining function.

## 3.1 The whole set of implants

In the first instance we considered the whole set of implants regardless for the position of implants in the mouth. From Table 3 we can see that globally there is a significant difference between the virtual planning implant position and the clinical actual position in the bone ($p''' = 0.02$). Furthermore we can see that this significant result is referred to the spatial $X$-coordinates, in particular for the apex ($p_{X_{apex}} = 0.00$, $p_{X_{entry\ point}} = 0.04$).

Table 3: Results on the whole set of implants.

| | Apex | Entry point | Global |
|---|---|---|---|
| Combined | 0.015 | 0.14 | 0.02 |
| X | 0.00 | 0.04 | |
| Y | 0.43 | 0.84 | |
| Z | 0.98 | 0.20 | |

## 3.2 Upper and Lower arch

In this section we split out the entire set of implants into two groups depending on the fact that they are positioned in the upper or in the lower arch of the mouth. Results are shown in Tables 4. We can see that globally there is a significant difference for implants in the lower part of the mouth ($p''' = 0.01$). Investigating on partial aspects we can see that differences refer both to apex and entry point (both combined p-values are significant: $p''_{apex} = 0.01$ and $p''_{entry\ point} = 0.04$). In particular at the apex, differences refer to the

$X$-coordinate ($p_{X_{apex}} = 0.00$) whereas at the entry point differences are mainly related to $Z$-coordinate ($p_{Z_{entry\ point}} = 0.02$) and slightly to $X$-coordinate $p_{X_{entry\ point}} = 0.06$.

Table 4: Results on the implants in upper and lower part.

| | UPPER | | |
|---|---|---|---|
| | Apex | Entry point | Global |
| Combined | 0.09 | 0.71 | 0.24 |
| X | 0.060 | 0.22 | |
| Y | 0.28 | 0.85 | |
| Z | 0.20 | 0.89 | |
| | LOWER | | |
| | Apex | Entry point | Global |
| Combined | 0.01 | 0.04 | 0.01 |
| X | 0.00 | 0.06 | |
| Y | 0.95 | 0.92 | |
| Z | 0.17 | 0.02 | |

### 3.3 Front and Back

In this section we split out the entire set of implants into two groups depending on the fact that they are positioned in the front (positions starting with 1,2,3) or in the posterior (positions starting with 4,5,6) part of the mouth. Results are shown in Tables 5. We can see that globally there seem to be not significant differences both for the front and back part ($p'''_{front} = 0.13$, $p'''_{back} = 0.15$ ). Further investigating on partial aspects we can see that in the front part there are significant differences for the $X$-coordinate both at the apex and at the entry point ($p_{X_{apex}} = 0.02$ and $p_{X_{entry\ point}} = 0.03$). Also in the back part of the mouth there is significant difference for the $X$-coordinate but only at the apex ($p_{X_{apex}} = 0.01$).

## 4 Conclusion

In this paper we evaluate the accuracy of the clinical results of dental implant positioned in total edentulous patients with CAD/CAM surgical guides produced after 3D software planning, by analyzing the discrepancies between the project position and the clinical position actually reached. Since data available from this study do not allow to consider traditional parametric technics we opted for nonparametric technics in the field of

Table 5: Results on the implants in front and back part.

| FRONT | | | |
|---|---|---|---|
| | Apex | Entry point | Global |
| Combined | 0.20 | 0.13 | 0.13 |
| X | 0.02 | 0.03 | |
| Y | 0.87 | 0.46 | |
| Z | 0.96 | 0.54 | |
| BACK | | | |
| | Apex | Entry point | Global |
| Combined | 0.07 | 0.35 | 0.15 |
| X | 0.01 | 0.44 | |
| Y | 0.35 | 0.35 | |
| Z | 0.99 | 0.31 | |

permutation tests. The results of the analysis highlight that there exist discrepancies between the planned and actual implant position. In general, from the analysis it emerges that the $X$-coordinate is that mainly subjected to errors, both for the apex and the entry point. In particular, it appears that errors are more evident for the implants in the lower part with respect to those in the upper part of the mouth. Furthermore, errors in the implants on the front part refers both to apex and entry point $X$-coordinate, whereas for those implants on the back of the mouth refers only to the apex $X$-coordinate.

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