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Research Paper
Dental Implants

The primary stability of two dental implant systems in low-density bone

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Abstract. Primary stability in low-density bone is crucial for the long-term success of implants. Tapered implants have shown particularly favourable properties under such conditions. The aim of this study was to compare the primary stability of tapered titanium and novel cylindrical zirconia dental implant systems in low-density bone. Fifty implants (25 tapered, 25 cylindrical) were placed in the anterior maxillary bone of cadavers meeting the criteria of low-density bone. The maximum insertion (ITV) and removal (RTV) torque values were recorded, and the implant stability quotients (ISQ) determined. To establish the isolated influence of cancellous bone on primary stability, the implantation procedure was performed in standardized low-density polyurethane foam bone blocks (cancellous bone model) using the same procedure. The primary stability parameters of both implant types showed significant positive correlations with bone density (Hounsfield units) and cortical thickness. In the cadaver, the cylindrical zirconia implants showed a significantly higher mean ISQ when compared to the tapered titanium implants (50.58 vs 37.26; $P < 0.001$). Pearson analysis showed significant positive correlations between ITV and ISQ ($P = 0.016$) and between RTV and ISQ ($P = 0.035$) for the cylindrical zirconia implants; no such correlations were observed for the tapered titanium implants. Within the limitations of this study, the results indicate that cylindrical zirconia implants represent a comparable viable treatment option to tapered titanium implants in terms of primary implant stability in low-density human bone.

Keywords: dental implant; titanium; ceramics; bone density; torque.

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Primary stability is an important basic prerequisite for successful implant placement. This is especially the case in low-density bone, where good primary stability is crucial due to the greater risk of implant failure[1,2]. Primary stability can be defined as the biometric stability achieved immediately after implant placement[3], and it can be influenced by various factors.

In the past, surgical protocols have been modified to achieve higher implant stability in poor quality bone by means of a stepped osteotomy[2] or condensing procedures[4]. Recent studies have increasingly focused on tapered implants[5] to improve primary stability under such conditions[6,7]. Compared to implants with parallel walls,

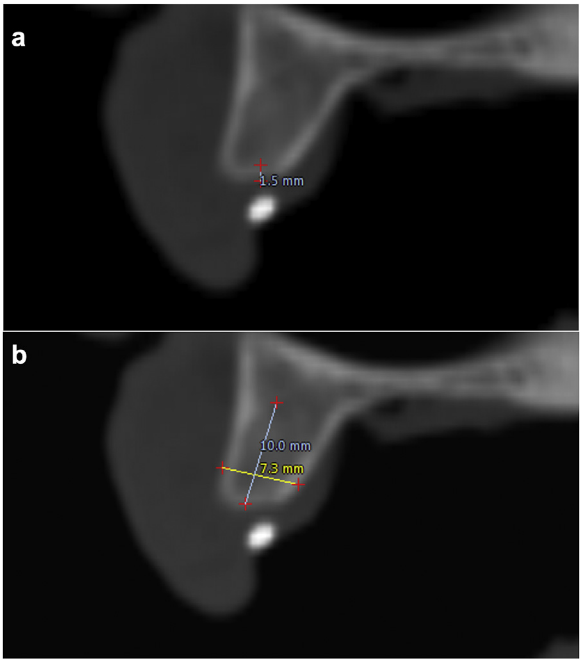

Fig. 1. Radiological measurements of (a) cortical bone thickness (mm) and (b) bone dimensions (mm) of the edentulous anterior maxilla. Gutta-percha points served as references for measurements and the subsequent placement of implants.

tapered implants favour primary stability due to the compressive forces they enact on the bone during implant placement[6,7].

In addition to the implant design, the implant material has also been considered to impact stability[8]. Due to the available long-term data, titanium implants are currently considered the gold standard for dental implantology[9]. However, zirconium oxide implants have shown comparable osseointegration to titanium implants in macroscopic as well as microscopic examinations[10,11], with aesthetic superiority in terms of their match to natural tooth colour[12]. Nevertheless, the literature currently lacks valuable data on novel zirconia implants in low-density human bone.

The bone density at the insertion site and the thickness of the cortical bone layer are patient-specific factors that also influence primary stability[13,14]. Therefore, preoperative assessment of the bone quality and quantity is essential to plan surgical treatment and select the appropriate implant design[2,15]. Computed tomography (CT) is an established method to assess these parameters objectively based on three-dimensional (3D) views and cross-sectional images[16]. Additionally, CT provides information on bone density via the Hounsfield units (HU) and thus enables a suitable analysis of the morphological and qualitative bone characteristics[13,17,18].

A commonly used clinical assessment of primary stability is the insertion torque value (ITV)[3,19–22], which measures the rotational friction between the implant and the bone. Additionally, the removal torque value (RTV) provides information about the bone–implant contact (BIC) area, as well as an insight into osseointegration[7]. Furthermore, resonance frequency analysis (RFA) is an established non-invasive and reliable procedure[4,6–8,20,23,24] that interacts with the BIC interface through a vibrational reaction; RFA findings are reported as the implant stability quotient (ISQ).

Thus, primary stability is influenced by multiple factors, and primary stability in low-density bone is of particular importance. The aim of this study was to investigate the influence of two different implant designs – novel cylindrical zirconia implants and tapered titanium implants – on primary stability in low-density bone. It was hypothesized that the novel cylindrical tissue-level zirconia implants (cylindrical zirconia) would have comparable primary stability to tapered tissue-level titanium implants (tapered titanium) in low-density cadaveric bone. Additionally, it was hypothesized that the effect of the compressive forces of the tapered titanium implants in low-density bone would be lower when cortical bone is present.

Materials and methods

After obtaining the necessary approvals from the Institute of Molecular and Cellular Anatomy of the University Hospital RWTH Aachen, the upper jaws of 14 fresh human cadaver heads (nine female and five male; average age 74.2 years, range 68–85 years) were prepared for radiological examination and implantation. The exclusion criteria were clinical signs of significant atrophy, insufficient bone for implantation, and teeth in the maxillary anterior region.

Radiological examination

Prior to CT examination, radiopaque No. 90 gutta-percha points (VDW GmbH, Munich, Germany) were attached to the gingiva in selected maxillary edentulous areas[2]. They were placed 10 mm apart using superglue at the reference points. Before implant insertion, CT scans with a slice thickness of 0.7 mm were obtained using a 128-row multi-slice CT scanner (Somatom Definition AS; Siemens, Erlangen, Germany). All radiological evaluations and processes were performed using established protocols[2,25].

CT data in DICOM format were imported into coDiagnostiX imaging software (Dental Wings, Montreal, QC, Canada) and measurements of cortical thickness and the CT grey values (which were measured in standardized Hounsfield units) were obtained. To enable reproducible measurements, an orthoradial adjustment was performed after screening the respective 3D datasets in the *X*, *Y*, and *Z* planes[4]. The total bone density (HU) was determined at a 90° angle to the bone surface and 5 mm from the crest of the ridge. Additionally, the thickness of the cortical bone was determined at each measurement point using software-based measurement tools. According to an established protocol[2], suitable bone specimens had a 10-mm vertical height, 5-mm buccolingual width, and 11-mm mesiodistal length (Fig. 1). A distance of 11 mm in mesiodistal alignment represents an adequate distance between implants[2]. After CT-assisted examination, nine of the 14 cadaver heads met the study requirements, and surgical implantation was performed in these cadavers.

Implant placement

Two different types of implant were used in this study: a tapered effect tissue-level implant made of titanium (length 8 mm, diameter 4.1 mm) and a cylindrical

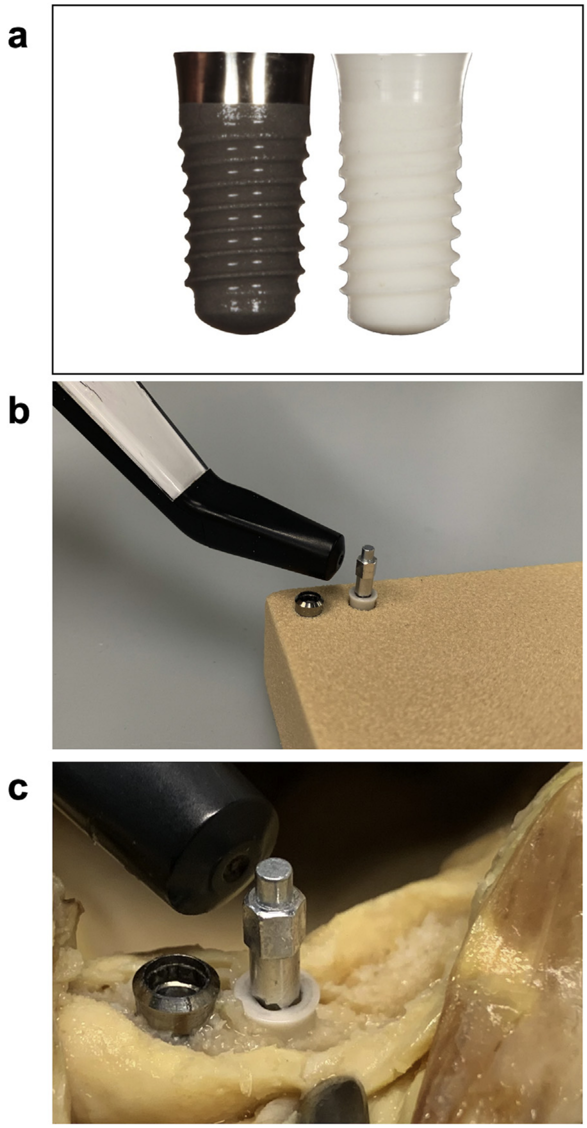

Fig. 2. (a) Titanium tapered tissue-level implant (left) and cylindrical zirconia tissue-level implant (right). Measurement of resonance frequency analysis in (b) polyurethane foam artificial bone block and (c) cadaver maxilla.

tissue-level implant made of zirconia (length 8 mm, diameter 4.1 mm). Both implants have the same thread pitch of 0.8 mm with comparable surface topographies (Institut Straumann AG, Basel, Switzerland; Fig. 2a). The maxillary bone was accessed via a surgical full-thickness flap with releasing incisions. No alveoloplasties were performed prior to implant placement.

The randomization of implant positions was performed according to the following procedure: an envelope with slips of paper was prepared for each cadaver head. On each slip of paper was a named implant position determined by CT. The slips of paper with the implant positions were drawn in a blinded fashion and alternately assigned to the cylindrical zirconia and tapered titanium groups. The implants were placed according to the manufacturers' instructions for each implant design using conventional drilling procedures, and the implant sites were prepared with a complete drilling sequence (using individual surgical pilot, twist, and profile drills with diameters of 2.2 mm, 2.8 mm, and 3.5 mm, respectively). In accordance with the manufacturer's drilling sequences, additional under-drilling of the apical extent of the socket was not performed for either implant type. The sites were drilled with a depth of 8 mm, which was checked using an implant depth gauge (Institut Straumann AG). Both implant types were placed with thread cutting, and implant placement was performed with an implant drive unit (Implantmed; W&H, Bürmoos, Austria). To prevent material damage, the maximum screw-in torque (i.e. ITV) and the maximum unscrewing torque (i.e. RTV) were limited to 50 Ncm[7].

After insertion, the primary stability of the implant was determined by means of the ITV, ISQ value, and RTV. The ITV was recorded during implant placement. The ISQ values were determined from measurements in four directions[26], by means of RFA and individual hand-screwed intelligent pins (Osstell, Gothenburg, Sweden; Fig. 2b, c). Three readings of ISQ values were taken and averaged. Finally, the RTV was determined using the implant drive unit[7].

To investigate the isolated influence of the cancellous bone on the primary stability of the respective implant systems, implant placement was performed into two different artificial bone blocks (#1522-01, #1522-03; Sawbones, Malmö, Sweden), which represent compromised and deficient bone density[27], based on a previous protocol[7]. These bone blocks are made of rigid polyurethane foam material, which has been approved by the American Society for Testing and Materials (ASTM F-1839-08).

Statistical analysis

Analyses were performed using GraphPad Prism version 7.0 (GraphPad Software, Inc., La Jolla, San Diego, CA, USA). Differences between ITV, RTV, and ISQ values were assessed with a matched paired *t*-test and Wilcoxon signed rank test. The correlations between implant type and ITV, RTV, ISQ, and bone parameters were evaluated using the Pearson correlation test. All data were recorded as the mean $\pm$ standard deviation (SD) values. Differences were considered significant when $P < 0.05$.

Results

A total of 150 implants were placed in this study: 25 tapered effect titanium and 25 cylindrical zirconia implants were placed in the anterior region of the maxilla in the cadaver heads, 25 implants of each type were placed in the artificial cancellous bone block with compromised density, and 25 implants of each type were placed in the artificial cancellous bone block with deficient density. The mean bone density of the alveolar ridge at the implant sites was 363.76 $\pm$ 61.01 HU (range 198–504 HU), and the cortical thickness was 1.59 $\pm$

Table 1. Descriptive parameters of maximum ITV, maximum RTV, and ISQ; mean ± SD values.

Type of implant		Maximum ITV (Ncm)	Maximum RTV (Ncm)	ISQ
Tapered titanium	Human cadaver maxillae	24.48 ± 6.64	18.52 ± 6.30	37.26 ± 14.52
	Artificial bone block[a]			
	Compromised bone quality	23.71 ± 1.90	20.00 ± 2.07	39.13 ± 6.67
	Deficient bone quality	7.28 ± 0.68	6.00 ± 1.04	27.87 ± 5.09
Cylindrical zirconia	Human cadaver maxillae	22.92 ± 5.79	17.52 ± 4.91	50.58 ± 9.68
	Artificial bone block[a]			
	Compromised bone quality	19.24 ± 3.56	15.33 ± 2.89	59.77 ± 3.21
	Deficient bone quality	5.96 ± 0.79	5.00 ± 0.41	42.56 ± 4.78

ISQ, implant stability quotient; ITV, insertion torque value; RTV, removal torque value; SD, standard deviation.
[a] Standardized low-density polyurethane foam artificial bone blocks (cancellous bone model).

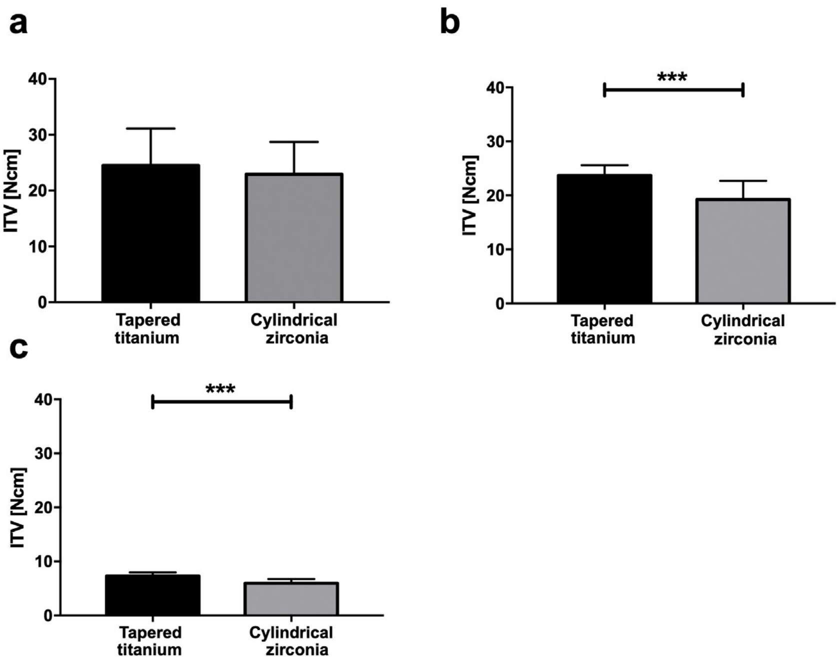

Fig. 3. Graphical representation of the mean maximum insertion torque values (ITV) for tapered titanium implants and cylindrical zirconia implants in (a) cadaver maxillae, (b) compromised density polyurethane foam artificial bone block, and (c) deficient density polyurethane foam artificial bone block. $***P < 0.001$.

0.41 mm (range 1.0–2.5 mm; see **Supplementary Material** Tables S1 and S2).

Descriptive parameters of maximum ITV, maximum RTV, and ISQ are reported in Table 1. Graphs showing the comparison of ITV, RTV, and ISQ between the tapered titanium and cylindrical zirconia implants are shown in Figs. 3–5, respectively. In both implant groups, the ITV were higher than the RTV. In the cadaver heads, no significant difference in ITV or RTV was observed between the cylindrical implants and the tapered implants. Conversely, in the artificial cancellous bone blocks, both the ITVs (compromised: 23.71 ± 1.90 Ncm vs 19.24 ± 3.56 Ncm, $P < 0.001$; deficient: 7.28 ± 0.68 Ncm vs 5.96 ± 0.79 Ncm, $P < 0.001$) and RTVs (compromised: 20.00 ± 2.07 Ncm vs 15.33 ± 2.89 Ncm, $P < 0.001$; deficient: 6.00 ± 1.04 Ncm vs 5.00 ± 0.41 Ncm, $P < 0.001$) were significantly higher for the tapered titanium implants when compared to the cylindrical zirconia implants (Figs. 3 and 4). Representative curves recorded by the implant drive unit during implant placement showed comparably increasing insertion torque and decreasing insertion speed in both groups (see **Supplementary Material** Figs. S1–S3).

The mean ISQ was calculated for both implant groups. The ISQ of the cylindrical zirconia implants ranged from 32 to 66.5, with a mean value of 50.58 ± 9.68 in the cadaver maxillae, which was significantly higher than the mean value for the tapered titanium implants (37.26 ± 14.52; $P < 0.001$) (Fig. 5). The Wilcoxon signed rank test showed that the cylindrical zirconia implants also had a significantly greater mean ISQ than did the tapered titanium implants in artificial bone with compromised density (59.77 ± 3.213 vs 39.13 ± 6.67, $P < 0.001$) and in artificial bone with deficient density (42.56 ± 4.78 vs 27.87 ± 5.09, $P < 0.001$) (Fig. 5).

Comparing the ITV, RTV, and ISQ of implants in the cadaver maxillae to those of implants in the artificial cancellous bone blocks with compromised and deficient density, it was observed that the ITV in the cadaver maxillae was higher than those in the cancellous bone model blocks, for both the cylindrical zirconia implants and the tapered titanium implants.

Significant positive Pearson correlations were found between the ITV and cortical thickness and between the RTV and cortical thickness for the tapered implants ($P < 0.001$, $r = 0.614$ and $P < 0.001$, $r = 0.668$, respectively) and cylindrical implants ($P < 0.001$, $r = 0.733$ and $P = 0.033$, $r = 0.427$, respectively) placed in the cadaver maxillae (Table 2).

A significant positive correlation was also found between the ISQ values and bone density (HU) in the tapered titanium ($P = 0.002$, $r = 0.564$) and cylindrical zirconia ($P = 0.002$, $r = 0.582$) implant groups (Fig. 6). For the cylindrical zirconia implants in the cadaver maxillae, Pearson correlation showed a significant positive correlation between ITV and ISQ ($P = 0.016$, $r = 0.416$), ITV and RTV ($P < 0.001$, $r = 0.672$), and RTV and ISQ ($P = 0.035$, $r = 0.424$). Although a significant correlation was found between ITV and RTV for the tapered titanium implants in the cadaver maxillae, no significant correlation was found between ITV and ISQ or between RTV and ISQ.

Discussion

This study is novel in comparing the properties related to primary implant stability between tapered titanium implants and cylindrical zirconia implants placed in poor-quality human cadaver bone and

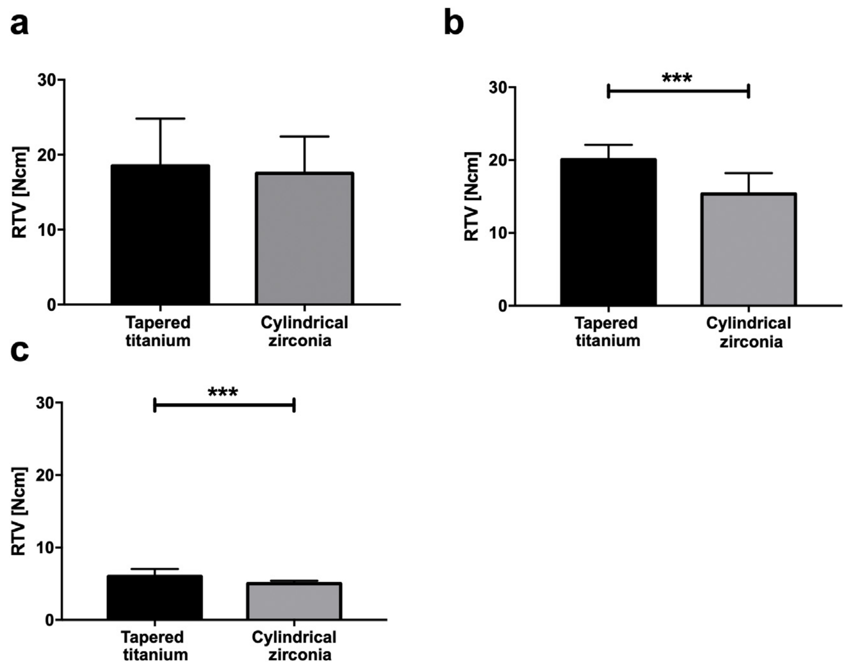

Fig. 4. Graphical representation of the mean maximum removal torque values (RTV) for tapered titanium implants and cylindrical zirconia implants in (a) cadaver maxillae, (b) compromised density polyurethane foam artificial bone block, and (c) deficient density polyurethane foam artificial bone block. $^{***}P < 0.001$.

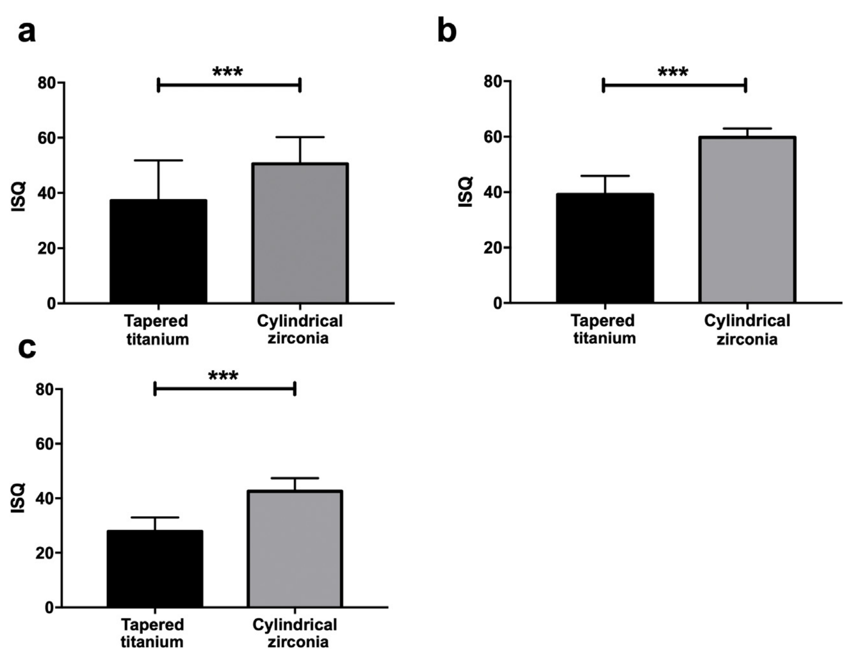

Fig. 5. Graphical representation of the mean implant stability quotient (ISQ) values for tapered titanium implants and cylindrical zirconia implants in (a) cadaver maxillae, (b) compromised density polyurethane foam artificial bone block, and (c) deficient density polyurethane foam artificial bone block. $^{***}P < 0.001$.

in artificial cancellous bone blocks of compromised and deficient density. Furthermore, the artificial bone blocks used served as a standardized control. The success of endosseous dental implants will depend on individual patient conditions and the parameters of the different implantation procedures. Additionally, many studies have shown that the survival rate of a dental implant is significantly influenced by its primary stability[3,6,8,19,20,28,29]. Turkyilmaz et al.[13] named several factors that influence primary stability, including implant design, implant geometry, and the quality and quantity of local bone.

Different classification methods have been proposed to assess bone quality, as the mechanical properties of bone are an important factor for successful osseointegration[14,27]. Friberg et al.[14] classified bone quality on the basis of macrostructures, determining the quality of the bone based on its morphology and the distribution of cortical and trabecular bone. In contrast, Misch[27] described a density-based bone classification in which subjective haptics detected with bone drilling determined bone quality. However, such bone quality classifications have significant limitations due to their subjective approach and they are therefore being replaced by more objective methods[2,13,17,18,25]. One such method is 3D CT, an established method for the objective assessment of bone density using Hounsfield units[13,17,18].

Bahat[1] described an increased risk of implant failure in low-density bone; therefore, primary implant stability in such bone plays an established role as a predictor of osseointegration[1,2,18]. In the present study, the cadaver bone had a mean density of 363.76 ± 61.01 HU, which is lower than the normal bone density values reported previously for the maxilla. Fuh et al.[18] described bone density of 516 ± 132 HU for the anterior maxilla, while Shapurian et al.[30] described bone density of 517 ± 177 HU in this region. Boustany et al.[2] also investigated the primary stability of implants in low-density bone, and found bone density values of between 173.4 HU and 312.1 HU. They attributed this deviation from the most common CT-determined jawbone densities to the formalin fixation of the cadavers[2], which is the most widely used method for embalming cadavers. This procedure has significant disadvantages in terms of increased stiffness, changes in tissue colour, and changes in tissue quality[31]. Therefore, to generate more realistic conditions (i.e. similar to those of living bodies), the present study used fresh body donors (the heads had been frozen immediately after death and no fixation solutions were used; they were later thawed). Since the focus of this study was on primary stability in low-density bone, not all cadaver heads were included in the study after bone density evaluation with CT imaging. Thus, the bone density values obtained in the

Table 2. Pearson correlation analysis.

Statistical correlation r (P-value)	Human cadaver maxillae		Artificial bone block[a] Compromised bone quality		Artificial bone block[a] Deficient bone quality	
	Tapered titanium	Cylindrical zirconia	Tapered titanium	Cylindrical zirconia	Tapered titanium	Cylindrical zirconia
ITV vs ISQ	$r = 0.315$ NS	$r = 0.416$ ($P = 0.016$)	$r = -0.001$ NS	$r = -0.077$ NS	$r = 0.414$ ($P = 0.039$)	$r = 0.398$ ($P = 0.049$)
ITV vs RTV	$r = 0.797$ ($P < 0.001$)	$r = 0.672$ ($P < 0.001$)	$r = 0.804$ ($P < 0.001$)	$r = 0.884$ ($P < 0.001$)	$r = 0.084$ NS	$r = 0.257$ NS
RTV vs ISQ	$r = 0.101$ NS	$r = 0.424$ ($P = 0.035$)	$r = 0.111$ NS	$r = -0.084$ NS	$r = 0.022$ NS	$r = -0.086$ NS
Bone density (HU) vs ITV	$r = 0.776$ ($P < 0.001$)	$r = 0.789$ ($P < 0.001$)	NA	NA	NA	NA
Bone density (HU) vs RTV	$r = 0.629$ ($P < 0.001$)	$r = 0.436$ ($P = 0.029$)	NA	NA	NA	NA
Bone density (HU) vs ISQ	$r = 0.564$ ($P = 0.002$)	$r = 0.582$ ($P = 0.002$)	NA	NA	NA	NA
Cortical thickness vs ITV	$r = 0.614$ ($P < 0.001$)	$r = 0.733$ ($P < 0.001$)	NA	NA	NA	NA
Cortical thickness vs RTV	$r = 0.668$ ($P < 0.001$)	$r = 0.427$ ($P = 0.033$)	NA	NA	NA	NA
Cortical thickness vs ISQ	$r = 0.219$ (NS)	$r = 0.475$ ($P = 0.017$)	NA	NA	NA	NA

HU, Hounsfield units; ISQ, implant stability quotient; ITV, insertion torque value; NA, not applicable; NS, not significant; RTV, removal torque value.

[a] Standardized low-density polyurethane foam artificial bone blocks (cancellous bone model).

present study by CT correspond to values of low-density bone.

The thickness of cortical bone varies between individuals and has a significant influence on the primary stability of implants[13]. In this study, the mean cortical thickness was 1.59 ± 0.41 mm. The study findings of significant positive Pearson correlations between ITV and cortical thickness and between RTV and cortical thickness, for both tapered titanium and cylindrical zirconia implants, underline this assumption.

Moreover, the effect of tapered implants on primary stability has been widely discussed. Compared to implants with parallel walls, the tapered shape can lead to favourable compressive forces during placement, resulting in higher primary implant stability[5–7]. In the present study, it was observed that tapered titanium implants were significantly superior to the cylindrical zirconia implants with regard to ITV and RTV in both of the bone models (compromised and deficient artificial cancellous bone blocks; all $P < 0.001$), which can be explained by the compressive forces during placement[5–7]. In contrast, in the cadaveric cortical bone, there was no difference in ITV or RTV values between the tapered titanium implants and cylindrical zirconia implants. These observations suggest that the effect of compressive forces of the tapered implants is lower in the presence of cortical bone. In contrast to other studies that have found tapered implants to be superior to cylindrical implants[6,7], the present study showed tapered titanium implants and cylindrical zirconia implants to be comparable in cadaveric low-density bone. In addition, although in the previous studies the tapered titanium implants initially showed favourable primary stability due to apical bone compression[6,7], their secondary stability in terms of BIC in the apical region was lower over the long term than it was for cylindrical implants[6]. Therefore, the observations of this study would need to be verified in a clinical study. Nevertheless, the investigations performed in the bone model should only be transferred to human bone with caution, since complex trabecular structures are not found within the artificial bone.

Different studies have shown that the implant design influences the correlation between ITV and ISQ[3,7,32]. The present study confirmed these findings for cylindrical zirconia implants, which showed a significant correlation between ITV and ISQ, ITV and RTV, and RTV and ISQ in the cadaver maxillae.

Conclusions about primary stability can be drawn from the comparison of the results of different methods to assess implant stability, including ITV, RTV, and RFA. Nevertheless, these measurement methods remain controversial[4]. In this study, the RTV were smaller than the ITV. According to Ting et al.[33], this phenomenon is based on the correlation between the RTV and the gripping volume. In contrast, the ITV depends on individual bone characteristics and bone compression[33]. Therefore, to compare the ITVs in the present study, maxillae that showed comparable bone densities in the CT measurements were selected.

Another established objective method to evaluate primary implant stability is RFA. RFA can be used to assess changes in the micromotion of implants, which may be associated with reduced implant stability. Therefore, RFA has been used widely to compare the implant stability of different implant geometries and materials[2,4,12,23,25,34]. In this study, a positive correlation was observed between the ISQ and bone density (HU) for both implant types, as well as a significant correlation between ITV and ISQ and between RTV and ISQ for the cylindrical zirconia implant design in the cadaver heads. RFA can detect differences in micromotion associated with different degrees of stability. Therefore, this method is often used to compare different implant designs in in vitro studies[7,23]. In the present study, the ISQ values of the cylindrical zirconia implants in the cadaver maxillae and in the artificial bone were significantly better than those of the tapered titanium implants ($P < 0.001$). However, Lachmann et al.[23] stated that the comparison of different implant types with RFA should be avoided and that RFA should be used exclusively for follow-up of the same implant. Despite the widespread use of RFA in comparative studies[6,7,25], this controversy indicates that the favourable results obtained with

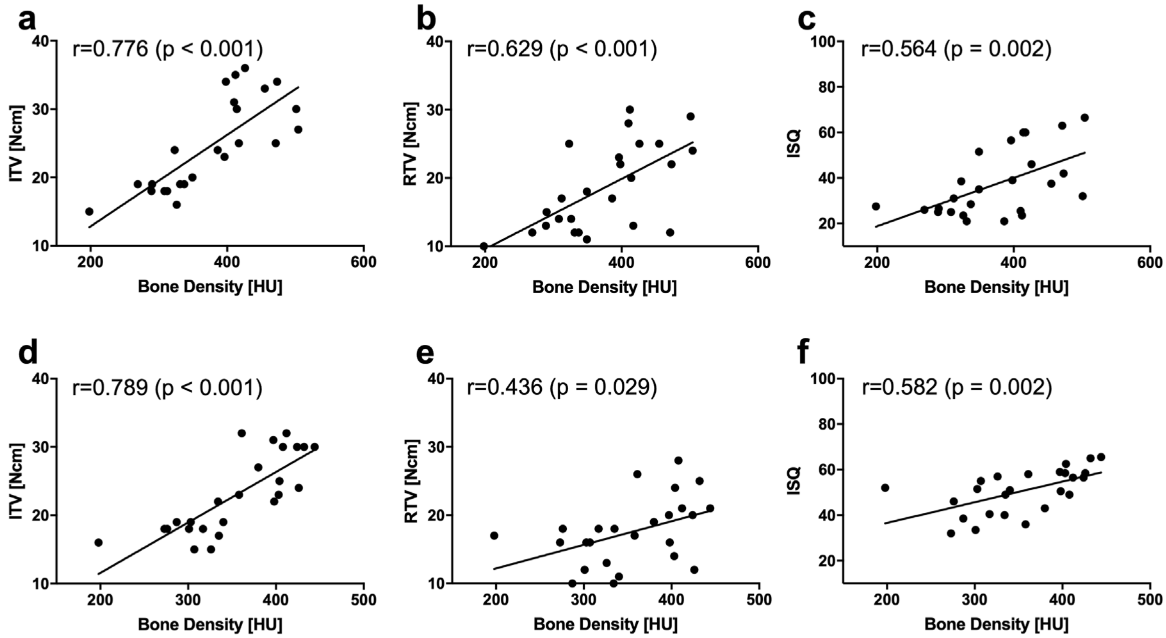

Fig. 6. Scatter plots of human cadaver bone density versus (a) ITV, (b) RTV, and (c) ISQ for tapered titanium implants; human cadaver bone density versus (d) ITV, (e) RTV, and (f) ISQ for cylindrical zirconia implants. (ITV, insertion torque value; RTV, removal torque value; ISQ, implant stability quotient; HU, Hounsfield units).

the cylindrical zirconia implants in the present study can only be viewed with caution. Consequently, the RFA method cannot be considered equivalent to ITV or RTV in the evaluation of the primary stability of an implant. Overall, though, these parameters represent different characteristics of the primary stability of an implant, based on which it appears that the cylindrical zirconia implants are comparable to and represent a viable alternative treatment option to tapered titanium implants in low-density bone.

Within the limitations of an in vitro study, the inclusion of two variables for the two different implant types – material (titanium, zirconia) and shape (tapered, cylindrical) – is a further limitation of this study. A precise evaluation of which variable ultimately resulted in the observed effects is not possible. The design of the implant thread has a significant influence on the stability of an implant. Although the two implant types differed in shape and material, both had an identical thread pitch and thread distance. The results presented indicate that the cylindrical zirconia implants represent a viable treatment option as an alternative to tapered titanium implants in terms of primary implant stability in areas of low bone density, in the cadaver. When implant placement was performed with these implants, ITV showed a positive correlation with ISQ, RTV, bone density, and cortical thickness. Although titanium implants achieved higher ITV and RTV values in the bone blocks, no difference between the two implant types was observed in the cadavers. Further clinical and long-term examinations are needed to confirm the hypothesis that the novel cylindrical tissue-level zirconia implants have comparable primary stability to tapered tissue-level titanium implants in low-density bone.

Funding

None.

Competing interests

None.

Ethical approval

According to the ethical approval given by the Ethics Committee of the Medical Faculty of RWTH Aachen, Germany (EK 219/16), institutional approval was obtained from the Institute of Molecular and Cellular Anatomy of the University Hospital of RWTH Aachen, Germany. All procedures involving human tissues were performed in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Patient consent

The donors on which this study was based provided permission during their lifetime for their bodies to be used after death for research and education purposes.

Data availability

All data generated or analysed during this study are included in this published article.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijom.2022.02.012.

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