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3D MEDICAL IMAGING ANALYSIS, PATIENT-SPECIFIC INSTRUMENTATION AND INDIVIDUALIZED IMPLANT DESIGN, WITH ADDITIVE MANUFACTURING CREATES A NEW PERSONALIZED HIGH TIBIAL OSTEOTOMY TREATMENT OPTION*

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High Tibial Osteotomy is frequently performed to correct varus knees misalignment and thus to prevent end-stage osteoarthritis. Traditional systems lack pre-surgical planning and custom-fit fixation plates. A new 3D printed system has been developed for a personalised surgical procedure. This starts with careful correction planning based on a standard preoperative long leg radiograph and a 3D scan of the knee by Cone-Beam CT, both in weight-bearing. From the latter, a 3D model of the proximal tibia is reconstructed, on which the surgery is planned. This allows the design of the surgical guide and fixation plate matching the tibial surface topology and 3D printed in medical grade titanium alloy using selective-laser-sintering. During surgery, the guided osteotomy and controlled opening mechanism ensure an accurate correction; this is stabilized with the custom-fit plate secured to the proximal tibia using locking screws of appropriate length. A final leg alignment to within 3° of the planned correction was achieved in 72% of cases. The surgical time was reduced by an average of approximately 30%. From medical imaging of the patient to product delivery to the hospital, the overall timeframe was about 15 days.

Keywords: High Tibial Osteotomy; Personalized devices; Custom-made; Surgical procedure; Medical imaging; Joint modeling; Weight-Bearing CT.

1. Introduction

In varus knees, the mechanical axis of the lower limb, i.e. hip–ankle line segment in the frontal plane, passes medial to the centre of the tibio-femoral joint, resulting in high compressive loads at its medial compartment [1-4]. As a consequence, cartilage wear and altered locomotion can be considerable impairments. In relatively young patients with this pathological condition in whom the cartilage in the medial tibial and femoral condyles is still not compromised, High Tibial Osteotomy (HTO) is frequently performed [5]. This is a surgical correction of the misalignment aimed to prevent end-stage OA [6-8], and to delay the more invasive total knee replacement. The open-wedge HTO is the most frequent option: an inclined osteotomy is performed at the proximal tibia, for a normal alignment of the knee to be restored, and an osteosynthesis plate with screws is used for final stabilisation. This allows the lower limb mechanical axis to pass much closer to the knee joint centre, thus restoring a physiological load distribution between the two compartments whilst preserving the original tibial plateau, thus potentially slowing down cartilage deterioration in the medial compartment [9].

Radiography is critical in the preoperative evaluation for HTO [10]. The multiplanar deformities of the distal femur, the proximal tibia and the knee joint require careful considerations, and a pre-operative plan of the limb alignment correction is essential [11]. Achieving the planned correction, i.e. the desired hip–knee–ankle (HKA) angle, is difficult, and also critical for the final outcome, which is highly dependent upon accuracy of this correction [12,13]. In addition, standard off-the-shelf plates [14] do not match the tibial bone surface topology after HTO, and the final overall thickness of the fixation system remains critical also for wound healing, with reported pain and soft tissue irritation around the plate [15,16]. A number of other complications have been reported [13,17,18]. Because of these concerns, some knee surgeons do not offer HTO to their patients.

To overcome these issues implied with the existing generic devices, a new personalised 3D printed system has been developed recently [18-20], whose mechanical safety has also been explicitly addressed [21]. The multiplanar deformities are addressed with an accurate 3D pre-operative planning of the surgical correction, based on medical imaging of each patient [18]. Consistent with this patient-specific plan, the instrumentation to control and to perform the correction, and also to apply the fixation system can now be designed and custom made. In the present work, the surgical guide and the fixation plate were both uniquely designed; these were then manufactured by a modern 3D printing process, using biocompatible metal powders, resulting in instrumentation with mechanical properties similar to those obtained by standard manufacturing, i.e. casting, but finally with an accurate matching to the underlying bone in each patient.

Instrumented gait-analysis was used largely to assess quantitatively the mechanical effects on the knee joint; [22,23] in a more recent publication from the present authors, [20] gait analysis and medical imaging were merged together for each patient to show ground reaction forces superimposed over the tibial plateau before and after surgery. In theory, a pre-operative gait-analysis can also enhance the pre-operative planning, by adding biomechanical criteria to the standard geometrical targets for the limb alignment.

The aim of the present study is to report on the overall procedure implied in the design, implantation and assessment of a novel custom-made HTO system. This includes original patient-specific knee joint modelling, planning of the corrections, design of the plate and cutting jigs, manufacturing via 3D metal printing process, surgical implantation and functional analyses. Improvements with respect to standard off-the-shelf systems were expected in a reduction of the surgical time [19] and in a higher overall accuracy.

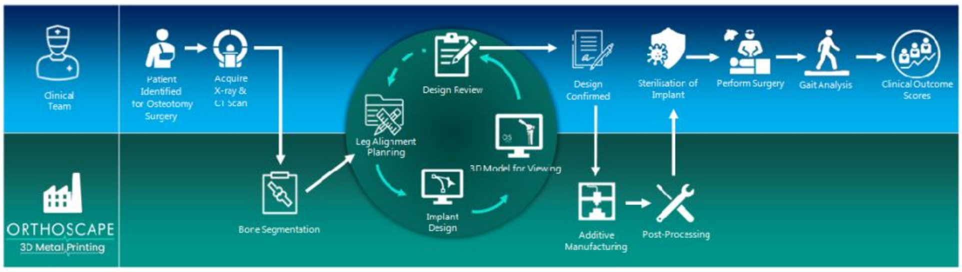

Fig. 1. Workflow for the entire procedure, distinguished for the activities performed in the hospital by the clinical team (above), and those in the company by the technical team (below)

2. Materials and Methods

The novel personalized system for HTO surgery was the TOKA (Tailored Osteotomy for Knee Alignment, Orthoscape, 3D Metal Printing LTD, Bath, UK), which uses patient-specific surgical guides and stabilisation plates, both 3D printed; for these, the geometry was generated according to a precise 3D pre-operative planning. The entire workflow of the procedure is reported in Figure 1, where those activities performed in the hospital and those in the company are depicted. Details of these various phases are described here below.

2.1. *The clinical cohort*

Patients were selected among those affected by early-stage medial knee osteoarthritis resulting from excessive joint varus and indicated for open-wedge HTO. Those reported in the present work were taken from a perspective cohort of 25 patients (age: 53.92 ± 7.3 years; gender: 6 females / 19 males; operated knee side: 13 left / 12 right; body-mass-index: 26.9 ± 4.2 kg/m^2) included in a clinical and radiological outcome measurement study still in progress; [18] the study received institutional review board approval, and informed consent was obtained from all individual participants. Inclusion criteria were: age between 40 and 65 years old, BMI under 40, varus knee malalignment and uni-compartmental medial non-inflammatory knee osteoarthritis.

2.2. *Medical imaging and bone modelling*

All patients received pre-operative radiological acquisitions to assess the degree of the deformity and to plan the appropriate angle of correction in 3D. The same images were acquired after HTO at 6-month follow-up to observe whether the desired correction was achieved, and the extent of the biomechanical effects at the lower limbs during locomotion. Standard full lower-limb weight-bearing x-ray imaging, and CT scans in weight-bearing were obtained for design purposes and lateral x-rays were used to quantify posterior slope change.

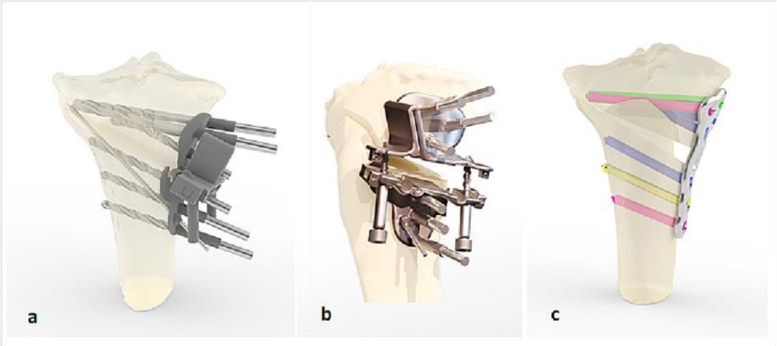

Fig. 2. Diagrammatic illustration of the TOKA system for custom-made HTO, in its three surgical steps: (a) the titanium alloy surgical guide in the correct position matching the underlying proximal tibia bone profile, to assist with the pre-planned drill orientations and bi-planar bone cuts; (b) the same surgical guide after the planned opening wedge correction achieved by the integrated screw-driven opening mechanism; (c) the custom-made titanium alloy plate to stabilize the osteotomy, secured in place to the proximal tibia, here using seven 5.0 mm locking screws.

A Cone-Beam CT device (Carestream, Rochester, NY-USA) was used to acquire the knee joint in its natural single-leg standing position. DICOM files were generated with a 0.26 mm slice resolution, and imported into image processing software (ScanIP 2018, Synopsys, USA). 3D reconstructions of the tibiae were generated using a 350 Hounsfield unit threshold and smoothing operations, and these bone models were then exported in STL format. These reconstructed 3D models of the proximal tibia were used in combination with standard X-ray imaging to quantify the pre-operative knee deformity, to fully plan the surgery before HTO, and to generate the surgical guide and fixation plate geometry for 3D printing manufacturing (Figure 2).

2.3. *Design of the custom HTO system*

The bi-planar osteotomy planes were manually positioned using computer aided design (CAD) software (Rhinoceros 7, Robert McNeel & Associates). The post-operative geometry was simulated by splitting the tibia about the osteotomy planes and rotating the proximal tibia fragment by the desired opening angle on the medial side. The rotation was about a hinge axis positioned in the bone remained at the lateral side of the tibia fragment, as determined and specified by the surgeon. The patient-specific cutting guide (Figure 2a) and plate were created using CAD software (Rhinoceros 7, Robert McNeel & Associates; Geomagic Freeform, 3DSystems, USA), taking into account the pre- and post-operative geometries to create an integrated opening-mechanism (Figure 2b). The region where the cutting guide was planned to contact the bone was based around the screw positions, with a 1 mm off-set from the bone surface to account for soft tissue. The cutting slots were positioned at the intersection between the osteotomy planes and the bone contacting surface, thus limiting errors in bone cuts due to inclinations of the blade. The planning software also calculates and records the length of the required screws. For each patient, gap opening angles together with locking screws to secure the plate (Figure 2c) to the bone were defined with the surgeon in the pre-operative 3D planning (see next section).

2.4. *Interactions with the surgeon*

The final 3D plan is the result of interactions between the design and engineering team of the company and the surgeon using digital planning. For the present study, the Miniaci method was used for the pre-op planning. [24] The surgeon determined the required correction, expressed as change in HKA angle (where > 180° is varus), or in medio-lateral intersection of mechanical axis (hereafter termed ML, expressed as a percentage of tibial plateau width, where ML = 0%, representing the medial border of the tibia), both based on the pre-operative weight-bearing long leg radiograph. The location and angle of the main incision together with any desired change in posterior tibial slope (PTS) were configurable during this 3D preoperative planning (Figure 3). The surgeon was also able to select the number, position, orientation and lengths of the 5.0 mm locking screws to secure the plate to the bone; this allowed possible careful plans around any existing hardware in the bone such as ACL repair screws or any unusual anatomical features. The planning software, therefore, reported the final predicted bone fragment positions, and the corresponding leg alignment (HKA and M-L) and PTS. The planning was iteratively refined if required to completely satisfy the requirements of the surgeon. Notably, in the vast majority of cases, the first planning proposed by the technical team was accepted by the surgeon. The final design and geometries of both the surgical guide and the stabilization plate were then generated utilising the patient's individual tibia surface morphology. The other output of the digital planning is the screw and drill length requirements. The final 3D plate design and surgical plan is provided in a prescription document to the surgeon for final signed approval.

2.5. *Manufacturing*

Once the final plan and design were approved by the surgeon, the surgical guide and plate were 3D-printed in medical grade titanium alloy (Ti6AL4V, ASTM F136 grade 23) using selective laser sintering according to an ISO13485-certified production process (AM250, Renishaw plc, Wotton-under-Edge, UK). [21,25] The powder particle size was between 15 and 45 μm, the laser power was 200 W and the layer thickness was 40 μm. The following laser parameters were used: 80 μm point distance and 50 μs exposure time for borders; 60 μm point distance and 50 μs exposure time for fill hatching. Four borders were used with a hatch offset of 160 μm.

The surgical guide embodies all the required instrumentation for the osteotomy; the entire kit including the guide, plate, drills and screws weighs approximately 0.3 kg. The guide incorporates a patented opening mechanism which removes the need for placing instrumentation, such as spreaders and osteotomes, within the osteotomy cut.

2.6. *Surgical technique*

All surgeries were performed by an experienced knee surgeon. [18] The patient, under regional anaesthesia supplemented with sedation, was positioned supine with a thigh tourniquet. The knee joint line position was identified by placing an intra-articular needle parallel to the surface of the tibial plateau. A longitudinal skin incision, approximately 6 cm in length, was made over the pes anserinus insertion at the anteromedial aspect of the proximal tibia. This was exposed by elevating the insertion of the pes anserinus and the hamstrings tendons, and by releasing slightly the superficial layer of the medial collateral ligament. The patient-specific cutting guide was placed in the planned position and temporarily secured with two k-wires, whose position was confirmed with intra-operative fluoroscopy; this allowed possible re-positioning of the guide before definitive placement, eventually secured with seven drill bits (Figure 3a).

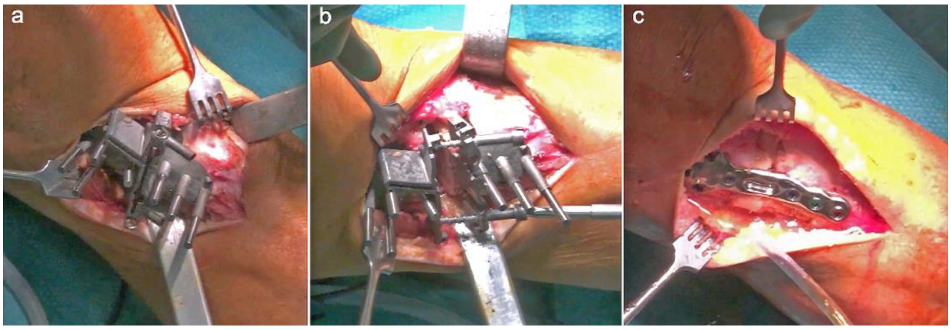

Fig. 3. Pictures taken in the operating theatre showing the various surgical phases, correspondent to those in Figure 2, i.e. (a) the jig in place; (b) the opening mechanism; (c) the plate in place.

The biplanar osteotomy was then performed (Precision Blade, Stryker), and the planned osteotomy gap was opened using the two opening screws (Figure 3b), temporarily stabilized with two patient-specific wedges. The cutting guide was then removed, leaving only the two drill bits above and below the osteotomy. The custom plate was positioned using the two remaining drill bits as a guide and fixed with seven screws. The two temporary wedges were then removed and an allograft bone wedge from the Rizzoli Orthopedic Institute bone bank was placed in the osteotomy gap (Figure 3c).

Following surgery, the knee was placed in an extension brace for three weeks, removable for the range of motion exercises, which were recommended from the second day after surgery. Following an initial non-weight-bearing period of three weeks, progressive weight-bearing as tolerated was allowed.

2.7. *Clinical, radiological and functional assessments*

Weight-bearing long leg radiographs and CT scan were repeated at 6 months follow-up for assessment of correction based on HKA angle, ML distance, and PTS. Patient-reported Outcomes (PROMS) [26] were taken pre-operatively, and at one, three, six, and twelve months post-operatively. The PROMS recorded were the Knee Osteoarthritis Outcome Score (KOOS), and visual analogue pain scores (VAS, 0=no pain, 10=worst pain). The KOOS was considered as a total score averaged across all domains and as individual domains. The VAS score was for pain during activity (VASact).

Instrumented Gait-Analysis was also performed prior to the surgery and at 6-months follow-up. A 9-camera motion capture system (Vicon®, Nexus motion-capture Software v.2.12.1, with B10 Bonita Optical cameras, Oxford, UK), together with two ground reaction force platforms (Kistler™, model 9291B, Winterthur, CH) and a wireless EMG system (Zerowire, Cometa, Milan, Italy) for the myoelectric activity of the main muscles of the lower limbs. An established protocol (IOR-gait) was used to position reflective markers on the skin in well-defined anatomical landmarks and to calculate 3D kinematics and kinetics of the hip, knee and ankle joints. [27] Traditional level walking was collected and analyzed as gait is the most common activity and it can reveal much of the biomechanics of the knee in locomotion.

CT data collected before surgery and at 6 months follow-up were also used for 3D morphological bone reconstructions through image segmentation, in particular to compare the achieved tibia correction with respect to the pre-operative planning using distance-map analysis. [28]

3. Results

The overall timeframe of the entire process outlined: from medical imaging to product delivery to the hospital, was about 15 days.

Modelling, planning, manufacturing, implanting, and assessing were performed in all surgical cases without any major problems. Since the procedure was planned based on the exact patient’s morphology, it was less invasive, particularly with regard to the incision length. In addition, due to the use of the custom surgical guide, no intraoperative measurements and fewer intraoperative radiological acquisitions were required reducing the surgical time by around 30% compared to conventional surgical technique.

The leg alignment correction was successful: the target correction of HKA at 0° ± 3° was achieved in 72% of all cases. As the larger discrepancies were mostly in the initial cases, the final 12 cases achieved 84% within ± 3° of the target correction. The mean discrepancy between the plan and the achieved in the final 12 cases was 1.2°± 1.4°

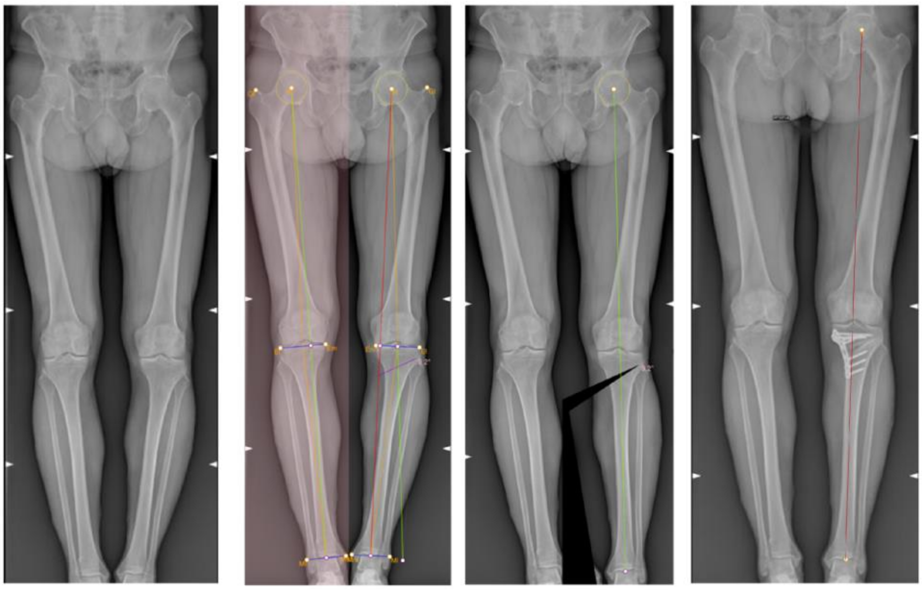

Fig. 4. Long-leg X-ray pictures of a left leg to be operated (left), two diagrammatic representations during the pre-op planning (centre), and the same leg after operation (right).

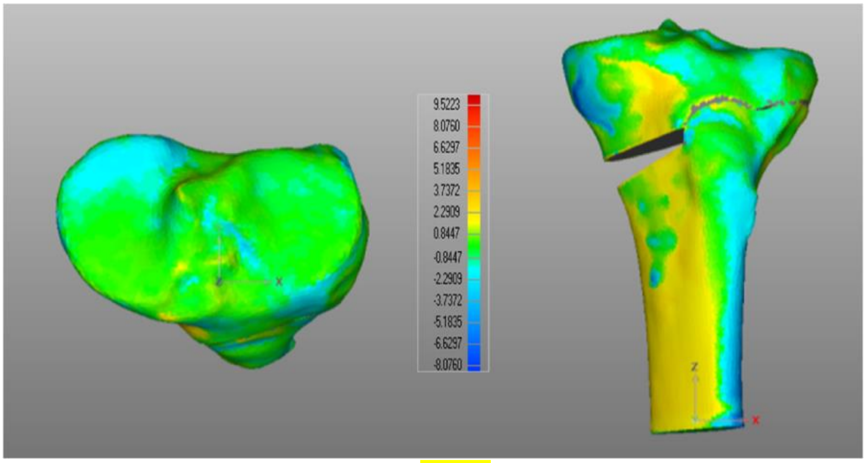

Fig. 5. Figure 5. Results of the distance-map analysis (in mm) of the proximal tibia from above (left) and from the front (right) in a typical patient.

The successful overall correction was observed also in terms of the medio-lateral intersection of the lower limb mechanical axis with the tibial plateau. The difference between the achieved and planned intersection, expressed as a percentage of plateau width (where 0% represents the medial border of the plateau) was 6.0 ± 6.1 % (min÷max -16.7 % ÷ 3.8 %). A typical case is shown in Figure 4.

Distance-map analysis between the planned and the post-operative condition (Figure 5) of the proximal tibia showed mean deviations smaller than 2 mm,[28] indicating good achievement of the planned alignment goal and, therefore, overall correction.

Gait analysis revealed correction after operation of the knee joint moments, in all three anatomical planes (Figure 6); a considerable restoration of the normal physiological pattern was observed especially in the frontal and transverse planes, with a full superimposition of these curves after operation to the control band data collected for age matched normal (i.e. no musculoskeletal pathology) subjects. [27]

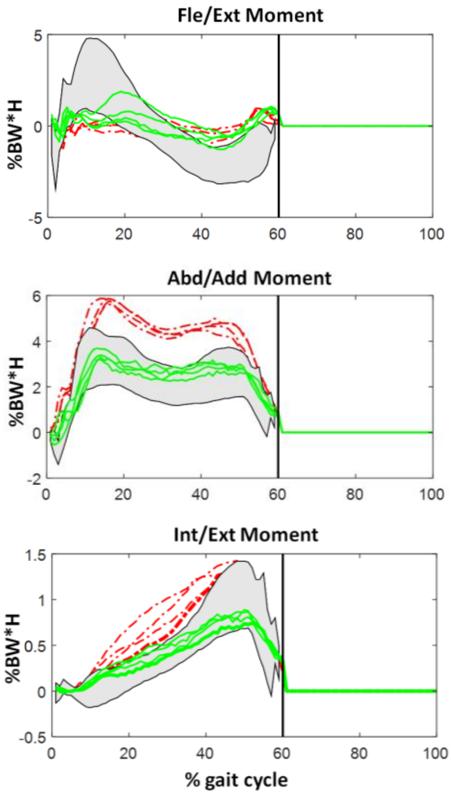

Fig. 6. Plots of the three components of the knee joint moment for a full cycle of level walking (from heel strike to heel strike; in the following swing phase the ground-reaction-force is null), from a typical patient, expressed as percentage of BodyWeight · Height: in the sagittal (top), frontal (central) and transverse anatomical planes (bottom); four repetitions before (red) and after (green) surgery are superimposed to corresponding control data [27].

4. Discussion and Conclusion

The present work reports on an original procedure for a novel custom-made HTO system, from medical imaging to clinical and functional assessments. The phases of the procedure include patient-specific modelling, planning and design; the result is a cutting guide and fixation plate which match the tibial profile before and after HTO, respectively. Both devices are produced with additive manufacturing using an established medical grade titanium alloy. The overall procedure worked very well and was performed successfully in 25 patients without major complications. Based on recent reports from the literature [18,29] of standard HTO systems, the present work shows higher overall accuracy, reduction as expected of the surgical time, better implant fit, and higher satisfaction of the patient associated with the rapid reduction of pain.

The present piece of work addresses reasonably a recent relevant clinical issue. HTO in fact has been demonstrated to successfully delay by more than 15 years the onset of end-stage knee arthritis and thus the need for total joint replacement. [30] The conventional procedure, however, has been associated with a number of complications, during and after surgery, such as deep vein thrombosis, nerve injury, chronic wound and bone fractures. [31] Without a careful plan and relevant jigs to guide the bone cuts and the opening wedge, under- and over-corrections occur frequently, affecting the long-term success of this surgical intervention. [32,33] Criteria for the optimal angular correction by HTO of a severely varus knee, i.e. the target HKA angle, have not been fully established, [31,34] but once these have been fully defined then an accurate patient-specific 3D approach must be available, particularly to improve the current accuracy, safety, and clinical outcomes. The present system also is the only one including a custom-made 3D-printed stabilising plate, the other studies reporting only patient-specific instrumentation for use with standard generic plates. [33,35-39]

The present procedure included state-of-the-art technologies, such as skeletal modelling tools, 3D metal printing, instrumented gait analysis etc. In comparison with current literature, the present results from the gait analysis concurred with what has been previously published in terms of proper realignment of the lower limb mechanical axis, and of restoration of physiological frontal plane knee moment after surgery.[22,40,41] In addition, a novel Cone-Beam CT device was used to reconstruct the 3D weight-bearing morphology of the knee. [42,43] Because of these features, a more realistic determination of the target for the alignment of the joint articular surfaces was performed, thus better supporting the surgeon to produce a more reliable pre-operative planning. Compared to traditional CT, the present Cone-Beam CT scans feature a bigger volume with a single rotation thus significantly reducing the acquisition time and the risk of image distortion caused by the patient movement. This results in more accurate and higher resolution images with a lower radiation dose (~5-10 mGy) compared to standard CT systems (~20-50 mGy). The presented procedure, however, does not require these advanced CT scans, and can also be performed using imaging from standard, non-weight bearing, CT systems.

Nevertheless, also according to recent literature on modern technologies for HTO, further thorough investigations on other aspects are suggested. [22,44] In addition to gait analysis, morphological reconstructions based on careful 3D bone models from advanced medical imaging and relevant biomechanical analyses, ideally including also finite element analysis, are recommended, especially for customized systems as in the present study. In this perspective, mathematical evaluations using distance map analysis should provide further evidence of the appropriateness of new customized surgical procedures, particularly in terms of achieving the overall surgical plan, and also of maintaining the plate-to-bone match over time.

The present technique was aimed at achieving a personalized and a more accurate opening wedge HTO procedure, [32] with reduced need for intraoperative radiology, navigation or robotic systems, [45,46] or any other additional measurement, by using only subject-specific instrumentation, i.e. bone drilling/cutting guide and implantable fixation plate. The overall accuracy of the present technique has been recently assessed carefully by the present authors in eight human cadaveric limbs, [25] and an excellent agreement was found between the planned osteotomy and the final surgical correction angle, with absolute mean error between the two of 0.3°. Those measurements [25] compared favourably to other patient-specific instrumentation investigated in similar studies, [33,47] and also demonstrated that 3D printed patient-specific cutting guides and custom plates can result in reliable methods of correction without additional expensive (and time-consuming) intraoperative technologies. In that publication it was also emphasised that pre-operative planning is essential for an accurate re-alignment, though the optimal correction can be challenging to achieve with standard operating techniques. [45] Current 3D computer-based planning software [24,48] can overcome the limitations of traditional two-dimensional geometric methods performed using long-leg radiographs based on anatomical and mechanical axes. However, the precise amount of correction is still debated, as it is recognised that under- or over-correction during HTO can lead to early failure. [12]

Clearly, the present work reports on relatively few clinical cases, but the scope was mainly to describe the overall procedure and multi-instrumental workflow; in the future, the present technique shall be applied to analyse a large population of subjects to confirm feasibility, safety and efficacy. In these preliminary cases the correct restoration of the leg alignment was assessed; in future more complete biomechanical analyses of the real lateral transfer of loads and relevant decompression of the medial compartment as achieved by HTO should be analyzed carefully. In the medium and long-term the more physiological load distribution over the tibial plateau should result ideally in a reduced rate of the osteoarthritis progression.

The current systems for patient-specific HTO, though limited to the surgical instrumentation, showed promising results at short- and mid-term follow-up, and thus encourage researchers to proceed further toward full personalisation of the surgical procedure. The present system addresses a simpler achievement of the accuracy of the alignment correction, a complete custom fit of the stabilising plate to also reduce complications in wound healing. The present new fully customized system with surgical guide and 3D-printed plate is addressing the unmet need of surgeons for bi-planar correction, feasible timing for production, a much simpler surgical procedure, a good final accuracy for the leg alignment correction, and excellent clinical outcomes. The latter, however, must be supported by thorough clinical trials, with long-term follow-up and a large number of patients, maybe investigating also the possible correlation between correction accuracy and clinical outcomes.

Author Contributions

Conceptualization, CB, AM, AL, HSG; Data curation, AG, GDF; Formal analysis, CB, AL, HSG; Investigation, CB, AG, GDF,SZ; Methodology, CB, HSG; Project administration, CB, AL,SZ; Validation, CB, AL, HSG; Visualization, AM, HSG; Writing - original draft, CB, AL; Writing - review & editing: CB, AM, AL, AG, GDF, SZ, HSG.

Ethical Compliance

This study was approved by the Ethical Committee of the 'Area Vasta Emilia Centro' (Cod. CE AVEC: 623/2019/Disp/IOR) at the request of the IRCCS Istituto Ortopedico, Bologna - Italy (Prot. Gen. 0013355 on 30/10/2019), and the clinical trial was registered at ClinicalTrials.gov (Cod.: NCT04574570). In detail, the authors certify that the institution approved the investigation protocol, and that investigations were conducted in conformity with all guidelines, regulations, legal, and ethical standards as required for humans or animals. Signed Informed consent for participation in this study and to publish related anonymized information/images was obtained by all patients. All patients were above the age of 18 years.

Conflicts of Interest

AM and HSG have shares in 3D Metal Printing LTD who market the TOKA device and are named on a related patent. The other authors have nothing to declare.

Availability of data/materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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