Clinical Study Protocol

An Open-label Single-arm Trial of a Novel Extramedullary Guide Coordinated with 3D Surgical Assistive Software for Total Knee Arthroplasty

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There is no assistive device for extramedullary surgery coordinated with 3D surgical assistive software for the total knee arthroplasty (TKA). We developed a novel extramedullary universal guide coordinated with 3D surgical assistive software and a novel extramedullary patient-specific assistive guide for the placement of femoral components by referring to an area not affected by cartilage or bone spurs, and filed a patent application. In this study, we visualize and reconstruct the total alignment of the lower extremity in TKA using these surgical devices, and validate their precision. A report releasing study results will be submitted in an appropriate journal.

Key words: total knee arthroplasty, 3D surgical assistive software, tibia, femur, extramedullary guide

Total knee arthroplasty (TKA) is estimated to have been performed in more than 612,000 cases in the United States and in approximately 82,000 cases in Japan in 2013, primarily for osteoarthritis, rheumatoid arthritis, and osteonecrosis of the knee.

In TKA, it is important to accurately cut the distal femur and proximal tibia, and to place the component (part of the artificial joint) at the right position and angle. This contributes to adequate load distribution, improvement of range of motion, alleviation of abrasion and loosening of parts, prolongation of the life of the prosthesis, and delay of its replacement. In addition, it is expected to eventually improve the patients' activities of daily living and quality of life.

With the conventional procedure, components are placed based primarily on the experience and intuition of the surgeon using 2D information provided by the anteroposterior and lateral X-ray images. However, it is difficult to accurately determine the position and angle of installation of the femoral or tibial components during surgery, and some reliable guide is necessary [1,2].

3D surgery using an assistive robot and navigation system is a solution to these problems, and several methods have been developed to facilitate this approach. In navigation surgery in TKA, it has been reported that osteotomy and implant placement are significantly more accurate than in conventional surgery [3]. However, the clinical efficacy of navigation surgery has rarely been reported. Moreover, there are many disadvantages, including large initial installation and

maintenance costs, the invasiveness of additional manipulations, such as antenna placement, the complexity of the procedure due to the necessity of averting the eye from the surgical field during the procedure to check the monitor, the prolongation of surgical duration, and the wide space occupied by the system in the surgical suite. Therefore, the adoption rate of 3D surgery still remains low. In many reports, it is concluded that 3D surgery is not different from 2D surgery, however in most cases, the postoperative evaluation method is not 3D evaluation but 2D evaluation by X-ray [4-6].

Recently, along with improvements in performance and reduction of the cost of computers, 3D surgical planning in a virtual space based on preoperative CT data, and computer simulation of osteotomy and installation of components of the artificial knee joint have become possible. Coordinating a 3D surgical plan based on simulation in a virtual space (preoperative planning) withsurgical assistive devices and then using this plan in actual surgery (intraoperative assistance) may be an effective method for improving the accuracy of surgery. Postoperative CT data can be compared with preoperative data in the same virtual space (postoperative assessment), and simulation of motion analysis is also possible. 3D surgical assistive software permits the consistent implementation of preoperative planning, intraoperative assistance, and postoperative assessment. At present, however, no extramedullary surgical assistive device coordinated with 3D surgical assistive software exists. We therefore developed a novel extramedullary universal guide coordinated with the 3D surgical assistive software package ZedView (LEXI Co., Tokyo), and filed a patent application (Fig. 1). In this study, we evaluated the accuracy of surgery using this device on the tibial side.

Several manufaturers have introduced Patient Specific Guides (PSGs) based on 3D CT preoperative planning to the market as an alternative for conventional methods of navigation. Precision osteotomy has become possible by using these guides, and the possibility of shortening the surgical duration and reducing the volume of hemorrhage has been suggested [7-9]. However, there have also been reports that the precision or duration of surgery has not changed compared with the conventional method [10-13]. As the design of PSGs varies among manufacturers, the precision may be affected by shapes that are more susceptible to the effects of cartilage and bone spurs [14].

Under these circumstances, we developed a novel extramedullary patient-specific guide for the installation of femoral components coordinated with the 3D surgical assistive software package ZedView, and referred to sites primarily in the anterior aspect of the distal femur not affected by cartilage or bone spurs. Nagoya Medical Center and ArthroDesign jointly
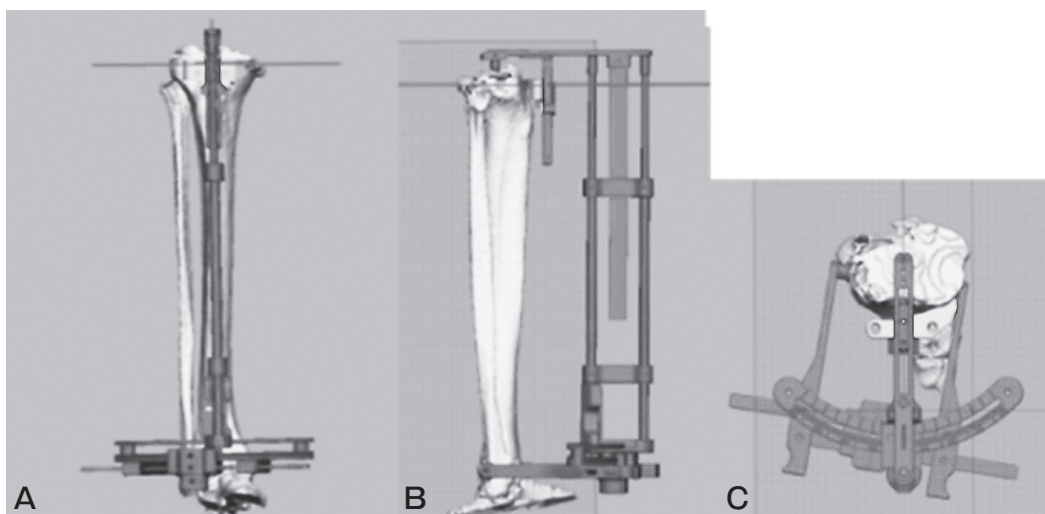

Fig. 1   The tibial-side universal guide based on the preoperative component installation plan using 3D support software. The universal guide is installed at the same time on the xyz coordinates of the selected tibial component based on the preoperative installation plan ((**A**) x (coronal)/(**B**) y (sagittal)/(**C**) z (axial)-axis)).

applied for a patent for the device. The devices were designed to be mutually coordinated by equipping PSGs with one of the relative goniometers as a marker for component placement. In addition, the surgical device, such as the novel extramedullary universal guide coordinated with 3D surgical assistive software, was equipped with another relative goniometer that was coupled with the goniometer on the PSG side to more readily simulate intraoperative conditions and navigate 3D surgical plans. By applying these surgical devices to the tibial and femoral sides, the total alignment of the lower extremity was visualized and reconstructed during TKA, and its precision was assessed.

Methods

Study design.   This study is a single center open-label single-arm trial that was approved by the Clinical Research Ethics Committee of Nagoya Medical Center (No. 2017-16), and registered in UMIN-CTR on September 19, 2017 (UMIN000029187).

Eligibility Criteria

Inclusion criteria.   (1) Patients with knee disorders due to osteoarthritis, rheumatoid arthritis, or osteonecrosis. (2) Patients expected to undergo TKA. (3) Patients aged 20 years or older at the time of informed consent. (4) Patients who are able to provide written consent based on their free will for participation in this study.

Exclusion criteria.   (1) Patients deemed unsuitable for participation in this study by study investigators. (2) Patients who have previously been registered in this study. (3) For the purpose of avoiding secondary infection, patients with, or suspected to have Creutzfeldt-Jakob disease.

Endpoints

Primary endpoint: Postoperative precision of installation (tibial component/internal-external rotation) compared with the 3D preoperative plan—namely, the proportion of cases in which the installation precision is confirmed to be within ±3° compared with the preoperative plan. The absolute difference between the preoperative plan and postoperative value will be also examined.

Secondary endpoints: 1) Postoperative precision of installation (the following components other than tibial component/internal-external rotation) compared with the 3D preoperative plan: femoral components (values of varus/valgus [3D functional axis], flexion/extension [3D functional axis] and rotation [Trans Epicondylar Axis (TEA)], distomedial, distolateral, medial posterior condyle and lateral posterior condyle values, and differences in x (coronal)/y (sagittal)/z (axial)-axis), and tibial components (values of varus/valgus [3D functional axis], anterior/posterior tilting [3D functional axis], tibial proximomedial and tibial proximolateral values, differences in x (coronal)/y (sagittal)/z (axial)-axis), and femoral-tibial components (femorotibial angle [FTA], hip joint extension angle and TEA-tibial anterior-posterior (AP) axis angle).

The absolute difference between the preoperative plan and postoperative value will be evaluated.

2) The incidence of adverse events will also be examined.

Preoperative plan.   CT scans of patients undergoing knee replacement surgery will be obtained. Next, the CT data will be imported into the 3D surgical assistive software package ZedView, 3D XYZ coordinates of the femur and tibia will be set, and STL data (3D morphology data) will be output. Based on these CT data and 3D data, the type and size of the femoral and tibial components of the artificial knee will be determined. After designing the position and angle of installation of each component, installation/adjustment parameters of surgical devices of the osteotomy guide will be calculated.

Intraoperative assistance (femoral side).   The devices will be adjusted according to the values of the installation/adjustment parameters of the surgical devices calculated from the results of computer simulation and PSG on the femoral side prepared from a real-size precut model of the femur. The devices will be sterilized, used in actual surgery, and, after osteotomy of the distal part of the femur, installed and used as reference marks for the installation of the femoral component.

Intraoperative assistance (tibial side).   Osteotomy of the proximal part of the tibia will be performed using the universal guide coordinated with 3D surgical assistive software, and the tibial component will be installed.

Intraoperative assistance (femoral side, tibial side).

The eventual total femorotibial alignment will be measured by using a relative goniometer to coordinate the PSG and the universal guide that is itself coordinated with the 3D surgical assistive software, measuring the position and angle of installation, and coordinating the position and angle with those on the tibial side. The motion range of the joint will be measured by simultaneously using the relative goniometers and Mobile Motion Visualizer AKIRA (System Friend, Hiroshima, Japan).

Postoperative assessment.   After surgery, CT scans will be obtained before discharge, and the accuracy of the position and angle will be assessed by 3D matching of the components between before and after surgery using the 3D surgical assistive software package ZedView. Kinetic analysis of the artificial joint along the time axis will be performed based on the exploratory data obtained with the relative goniometers and Mobile Motion Visualizer AKIRA.

Prohibited concomitant therapy.   Anticoagulation therapy on the day of surgery is prohibited in order to avoid major bleeding during surgery.

Statistical Consideration

Statistical analysis.   Analysis of primary endpoint: The proportion of cases in which the precision of installation in terms of rotation of the tibial component is confirmed to be within 3° compared with the preoperative plan and its exact 95% confidence interval (CI) will be calculated. Furthermore, the exact binomial test for the null hypothesis that the proportion is less than 40% will be performed. As a secondary analysis, summary statistics will be calculated for the preoperative plan, postoperative value, their difference, and the absolute value of the difference.

Analysis of secondary endpoints: Because the precision of postoperative installation will be compared with the 3D preoperative plan, the absolute values of the differences between the preoperative plan and the postoperative values will be calculated for components other than tibial component/internal-external rotation, and their summary statistics and 95% CIs will be calculated. Frequencies of adverse events will be also summarized.

Sample size.   In the observational study conducted at Nagoya Medical Center from July 2013 to December 2016, 29.4% (5/17 limbs) of the patients who underwent TKA without the universal guide were

confirmed to have an installation precision of within 3° compared with the preoperative plan, in terms of rotation of the tibial component. The threshold value was set conservatively at 40%. On the other hand, from the observational study, this value was 94.1% (32/34 limbs) in patients who underwent TKA using the universal guide, and thus the expected value in this study was set at 90%.

Adopting a statistical power of 0.90, 10 cases were needed to guarantee that the exact lower limit of the 95% CI of the proportion of cases in which the precision of installation was confirmed to be within 3° compared with the preoperative plan would be higher than the threshold value. In consideration of the possibility of non-assessable cases and the need to perform an exploratory evaluation of secondary endpoints, the target number of subjects was set at 20.

Discussion

In this study, TKA will be performed using an extramedullary universal guide coordinated with 3D surgical assistive software in patients with knee disorders who are expected to undergo TKA, and the efficacy and safety will be assessed. With this procedure, the risks of complications associated with intramedullary insertion of the rod, such as hemorrhage, embolism, and infection, may be reduced, and the precision of surgery may be improved compared with the conventional method of using 2D intramedullary rods. In addition, compared with a navigation approach, the procedure may make additional invasion due to antenna installation unnecessary, have similar precision, shorten the duration of surgery, and reduce the volume of hemorrhage. It will also make it possible to validate the postoperative precision of installation compared with the preoperative plan based on consistent preoperative and postoperative CT criteria.

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