## *SNUCM/SNUH IRB*

**Seoul National University College of Medicine/Seoul National University Hospital**
**Institutional Review Board**

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*IRB Decision Notification Document*

IRBNO : H-1506-037-670

RESEARCH TITLE : Randomized controlled trial: Comparison of ultrasonic osteotome and conventional drill osteotome (SONO Study)

INVESTIGATOR : CHUN KEE CHUNG

SPONSOR :

REVIEW LIST:

1. Protocol ver1.3
2. Information Sheet and Informed Consent
3. Case Report Form
4. IB
5. Curriculum vitae of Principal Investigator
6. Indemnification Provisions for Subjects

Review Comment:

According to [the IRB Approval Criteria], the IRB approves the research.

ALL CONDITIONS OF APPROVAL PREVIOUSLY ESTABLISHED BY SNUCM/SNUH IRB FOR THIS RESEARCH PROJECT CONTINUE TO APPLY.

CONTINUING REVIEW REPORT INTERVAL: ( 12 ) Month

IF YOU HAVE ANY QUESTIONS, CONTACT SNUCM/SNUH IRB (Tel: 82-2-2072-0694)

This is to certify that the information contained herein is true and correct as reflected in the records of the SNUCM/SNUH IRB. **We certify that SNUCM/SNUH IRB is in full compliance with Good Clinical Practice as defined under the Korean Ministry of Food and Drug Safety (MFDS) regulations and the International Conference on Harmonisation (ICH) guidelines.**

Byungho Park

**Chairperson**

2015-06-15

**Date**

All investigators performing SNUBH IRB approved projects must comply with the followings:

1. Enrollment of participated subjects before the IRB approval of protocol/protocol amendment is forbidden.

2. To conduct the study according to the approved protocol. To conduct the study differently from the original protocol is forbidden.

3. To use the approved Informed Consent Form.

4. The informed consent process shall be conducted based on sufficient explanation under no coercion or unfair influence, and a potential subject shall be provided with sufficient opportunity to consider the study participation.

5. Except for the unavoidable cases to protect subjects during the study conduct, any amendment of the study shall be implemented after getting the prior approval of the Board, and any amendment taken in an emergency situation for protection of subjects shall be immediately reported to the Board.

6. In case the study should be conducted differently from the original protocol since the immediate risk factor occurring to subjects should be eliminated, the amendment item that may increase risk factors occurring to subjects or have serious effects of the study conduct, items on the unexpected serious adverse drug reaction, or items on new information that may have negative effects on subjects' safety or study conduct shall be promptly reported to the Board.

7. The subject recruitment advertisement approved by the Board shall be used.

8. The Board approval period may not exceed one year. In case of intending to continue the study for more than one year, you are required to submit an annual continuation report.

9. In case the IRB review decision is not an 'Approval', written response for IRB decision result shall be submitted within six months since the IRB review date.

10. In the case of a decision by the Board to disapprove, you may have the opportunity to submit an appeal in writing. However, you should not file an appeal 2 times in a row with the same reason.

11. When completing the research, Study completion report and Study result report shall be submitted.

12. You shall comply with Bioethics and Safety Act, Pharmaceutical Affairs Act/Medical Device Affairs Act as defined under the Ministry of Food and Drug Safety (MFDS) regulations, the International Conference on Harmonization (ICH) guidelines and the Declaration of Helsinki.

13. According to the Declaration of Helsinki, all clinical studies shall be disclosed in the database that allows public access(primary registry) prior to the first subject enrollment; for example, you may use http://register.clinicaltrials.gov. For details, please refer to the IRB website.

14. The internal audit or inspection from the regulatory agency for the approved study could be conducted. Investigator shall cooperate in helping this to carry out, when requested for reading of study document (including electronic document) by internal auditor or monitor from sponsor, or inspector from regulatory agency.

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## Study protocol

### Patient population and randomization

The present study included patients for whom COL was planned with 1) cervical myelopathy at 3 or more levels due to spondylosis, congenital stenosis, or OPLL; 2) aged more than 20 years; and 3) with American Society of Anesthesiology physical status class 1 or 2.[27] The exclusion criteria were as follows: 1) concomitant neurological disease such as cerebral palsy or amyotrophic lateral sclerosis; 2) concurrent cancer or infection; 3) previous cervical spinal surgery; 4) a trauma-associated lesion; 5) inability to be followed up; and 6) refusal to participate in the study. The proportions of fusion failure were assumed to 30% and 10% in laminoplasty with a conventional drill and with a UBS.[12] To provide a power of 80% with a two-tailed significance level of 0.05, 72 patients for each surgical method were required.[12] Considering a drop-out rate of 25%, 95 patients in each group were enrolled. A computer-generated variable randomized block design was used for randomization and a research nurse independent of this trial provided randomization with concealed assignment. A total of 190 patients were equally allocated to one of two treatments (Fig. 1). The attending surgeons, patients, and staff members in the operating room were blinded to the surgical method until the day of surgery. Recruitment of patients started in July 2015 and ended in February 2018.

### Statistical analysis

Continuous data were summarized as mean or median (min, max) values depending on normality. Categorical variables are summarized as frequency (%). The analysis for the primary outcome was performed on data from the intention-to-treat population, which included all subjects who were randomized. Since about 14% of subjects missed the CT to assess bone union at 6 months, multiple imputation was applied. Five multiply-imputed data sets were created using a monotone logistic regression model. The variables in Table 1 were included in the imputation model. A sensitivity analysis was performed with the subjects who received a CT scan at 6 months, who were defined as the per-protocol population. The union rate was compared between the drill group and the UBS group using logistic regression. Because each subject had several laminae, logistic regression with the robust sandwich covariance estimate was used to account for the correlation among laminae within a subject.

Secondary outcomes were compared using the chi-square test for non-continuous values and the t-test or Wilcoxon rank-sum test for continuous values.[21] A linear mixed model was used for clinical outcomes to evaluate between-group differences and changes during each postoperative period compared to the preoperative point, and adjusted p-values were evaluated using the Bonferroni method. The fixed effects were group, time, and the interaction between group and time. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA), and statistical significance was defined as $p < 0.05$ (two-sided).