Responses to the comments of Reviewer A

Comment 1: I am concerned about one of the definitions of “success” – a return to normal voiding (<8 voids/day). This is a tricky outcome as you could conceivably have a patient who voids 9 x/day and after the intervention voids 7x/d. Is this really a success? Looking at your data it seems unlikely that you had any patients like this but it is still a concern. Did you have any patient who had only a modest decrease in voids/day but crossed that threshold of 8 who were thus counted as a success?

Reply 1: We totally understand your concern. Please allow us to make the following explanation first. In the definitions of success of “a return to normal voiding (< 8 voids/day)”, “< 8 voids/day” is based on “return to normal voiding”. When we judge the success of patients’ improvement, we would not only pay attention to the number of micturition but also pay attention to other variables, such as volume and urgency. Yes, we do have two patients whose frequency decreased by less than 50% from baseline but < 8 voids/day who were thus counted as a success. The average frequency of these two patients was 12 voids/day and 14.6 voids/day before the operation, and 6.8 voids/day and 7.6 voids/day after the operation, respectively. Although the improvement of urinary frequency was less than 50%, they basically returned to normal voiding. After the treatment of SNM, the average volume/void of these two patients increased from less than 150ml/void to about 300ml/void, and their urgency symptom was also improved. Therefore, we counted them as success.
Changes in the text: Yes. A revision has been made in Page 10 Line 196-199.

Comment 2: A scale measuring interference with life was utilized. Has this been validated? Has it been used elsewhere?

Reply 2: Yes. The scale of OAB-q was assessed using the validated International Consultation on Incontinence Modular Questionnaire (ICIQ)-OABqol. It has been cited by 136 articles. We have added a description of the source and added a reference in the methods. Thanks a lot.
Changes in the text: Yes. A revision has been made in Page 8 Line 153-154.

Comment 3: What do you mean that success was 79% for oab symptoms – 69% for uui and 42%
for uf? Where does the 79% come from?

Reply 3: Sorry for the trouble. OAB response was defined as either ≥ 50% improvement in any of the symptoms (frequency, urgency, and/or urge urinary incontinence) or average voids/day return to normal voiding (< 8 voids/day). UF response was defined as ≥ 50% improvement in voids/day or average voids/day return to normal voiding (< 8 voids/day). UUI response was defined as ≥ 50% improvement in leaks/day; Analysis only for patients with UUI. Those definitions have been described in the legend of Figure 2 (Page 25 Line 490-496).

Changes in the text: No.

Comments 4: Your population had a baseline number of voids per day of 29. That is extremely high even for an OAB study. How do you explain that?

Reply 4: The main reasons for this may be as follows. First of all, Chinese people have a relatively high tolerance for suffering. Most patients come to the hospital only when their symptoms are relatively serious, and the patients in our study are no exception. Secondly, there is a treatment method in China called acupuncture. Acupuncture can effectively improve the symptoms such as urgency, frequency, and nocturia, but it is cheaper than SNM. Therefore, patients with OAB symptoms prefer receiving treatment with acupuncture first and then further seek invasive surgical treatment after the effect of acupuncture is poor, which will undoubtedly intercept some patients with relatively mild symptoms.

Changes in the text: Yes. Page 12-13 Line 232-248.

Comments 5: There were a large number of patients lost to follow-up but the authors do acknowledge that.

Reply 5: Thank you for the comment. To be much clearer and in accordance with the reviewer concerns, we further explained the reasons for the lost (Page 16-17 Line 330-339).

Changes in the text: Yes. Page 16-17 Line 330-339.

Response to the comments of Reviewer B

Comment 1: Introduction

The introduction of this manuscript is unnecessarily long. It requires stylistic changes. Essentially, the following points need to be presented in a more concise manner:

I. Sacral Neuromodulation is a minimally invasive, effective means of treating refractory OAB.
II. For optimal relief, patients will require reprogramming of their neuromodulation device. The standard current protocol involves patients coming into clinic; however, this may be a barrier
to healthcare due to time and costs of traveling.

III. The BetterStim is a sacral neuromodulation device that may be programmed remotely. It may provide a solution to addressing clinic visits for programming.

IV. Short term results for urinary symptom relief with BetterStim are promising. This manuscript will present more long-term results with regards to the use of BetterStim in refractory OAB.

Reply 1: Thank you for the suggested. This part was revised and modified according to the comment.
Changes in the text: Yes. Page 5-7 Line 70-125.

Comment 2: This study appears to be an extension of a previously published study looking at the effects of BetterStim on refractory OAB. The authors mention that detailed study design has been previously mentioned; however, certain points must be included in this manuscript as well. These include
I. Time window for refractory OAB patients receiving BetterStim
II. What did reprogramming consist—adjustments to voltage, frequency?
III. Demographic data—distance to clinic, cost to travel to clinic

Reply 2: We are grateful for the suggestion. According to the suggestion, we added the following contents in the manuscript.
I. Time window for refractory OAB patients receiving BetterStim (Page 8 Line 141, and Figure 1).
Changes in the text: Yes. Page 8 Line 141.

II. Added a description of what reprogramming consist: At each visit, we would adjust stimulation parameters according to the needs of patients. Adjustments may include stimulation amplitude, frequency, pulse width, etc.
Changes in the text: Yes. Page 8 Line 148-150.

III. Added a description of the evaluation method of postoperative follow-up burden. And the results are added in Table 1.
Changes in the text: Yes. Revision have been made in Methods (Page 8 Line 143-145) and in Table 1(Page 27 Line 512).

Comment 3: Results
Data on distance to clinic should be highlighted as well.

Reply 3: We added the data in Table 1.
Changes in the text: Yes. Page 27 Line 512.

Comment 4: Discussion
Was there any reason that one-third of patients stopped following up? Was any attempt made to contact them? This is a significant proportion of patients.

Reply 4: Thank you for the comment. To be much clearer and in accordance with the reviewer concerns, we further explained the reasons for the lost (Page 16-17 Line 330-339).
Changes in the text: Yes. Page 16-17 Line 330-339.

Comment 5: Line 204-223— The purpose of this part of the manuscript is unclear. The authors discuss that sacral neuromodulation is typically used for wet OAB; however, in the introduction it is stated for the use of refractory OAB. In addition, there is a point made that 30% of the study population had interstitial cystitis. How was interstitial cystitis diagnosed in this group of patients? It is significant that nearly one third of the study population is also diagnosed with IC, but what significance?

Reply 5: Sorry for the trouble. We have modified this part to make it clearer and more focused.
Changes in the text: Yes. Page 12-13 Line 232-248 (added) and Page 14-15 Line 287-310 (deleted).

Comment 6: Was there a difficult learning curve for remote programming? At the end of year 3, were reprograms with significant changes, or more minute changes?

Reply 6: The operation of the remote programming is very simple. The hardware of the Patient Client of remote programming system consists of three parts: an app in the patient’s cellphone, a Bluetooth patient programmer, and an in vivo sacral stimulator. As long as the patients can operate the smartphone, the remote parameter adjustment can be completed once by a brief introduction. We only analyzed the changes in the number of reprogramming events. Every year, it has decreased exponentially. But the reasons for the decrease are still unclear. We think it is really a good idea to study the changes of reprogramming, including the changes of parameters adjustment, and it is worthy to be further investigated. Thanks a lot for this enlightening idea.
Changes in the text: No

Comment 7: Line 239: You mention that telephone followups lead to poor compliance; however,
the opposite argument can be made that clinic visits for OAB have poor compliance. One American study demonstrated that 40% patients do not followup with clinic visits.

Reply 7: Thank you for the comments. We think that although the success rate of telephone follow-ups is higher than that of clinic visits, the patients’ cooperation with data collection is much lower, which leads to the need to call patients many times to ensure the integrity of the data. This may be a subjective evaluation and needs further verification, so we deleted the description.

Changes in the text: Yes. Page 17 Line 344-346.