Peer Review File

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This is an interesting manuscript using a conceptual robot developed for retinal surgery using a novel RCM to achieve a precision of 10 μ m. The study is composed of two parts, making use of a simulator and an attempt at cannulation in donor pig eyes.

<u>Comment 1: While it is not the subject of this paper, knowing a little more about the robotic</u> system and any lag time in the realignment of the RCM would be of benefit. Does this lag time influence the duration of the surgical manipulation?

Reply 1: Thank you for your comments. For the realigning of the RCM, the calculating for the new RCM point cost about 5 ms, while the communication time from the force sensor to the control board was less than 1 ms. During the mast-slave control period, the new RCM point used at the next step was calculated by the force value, and the positions of the joints were read at the previous step. Thus, the lag time of the RCM realignment was only 6 ms, which could hardly influence the whole control loop. We have supplemented this part of the contents in Page 13, lines 241-247.

It is also mentioned that the force sensors register the forces used and in real-time modify the RCM strategy for the surgical application. If this is the case, for each surgeon, there needs to be an adaptation to his surgical ability and style, which suggests that a certain amount of time has to be spent before the experiment for the computer to correctly adapt to the surgeon. Is this the case, and how much time does it take. A better description of the whole experiment preparation time, and the conduct of the simulation would be very useful to better understand how the system functions. Schematics would also be useful.

Reply 1: Thank you for your comments. Participants in robot-assisted groups needed to be familiar with the robot operation until they could control the robot instrument manipulator following the instructions (The settled instruction was from the researcher to verify participants' familiarity with the robot). Because the ergonomic design of the robot makes it easy to operate, most participants could adapt to the robot operation rules within 20 minutes. We have supplemented this part of the description in page 8, lines 127-129. We have also added the schematics (Fig. 1)

Methodology:

since 3 repetitions of each test was done, are the results per test subject the average of these three repetitions or did you take the last measurement, and the first 2 are training? Is there any learning curve and is in fact your computer system learning from the first 2 how to adjust the RCM?

Reply: Thank you for your comments. After consulting the statistician, we found that the trim mean calculation method accords with the design of this study. The outlier (the greatest difference value) of three repetitions was removed and took the average of the two close results. (Page 10, lines 163-165).

The new RCM point used at the next step was calculated by the force value and the

positions of the joints read at the previous step. The calculation was based on the robot's current position and adjusted in the direction of reducing the force between the trocar and the tool. Since this part is not the subject of this paper and we are preparing another paper about the algorithm of the RCM adjusting, the detailed description of this part is not included.

Regarding outcomes, instead of three, you in fact have four: in the first you are looking at the time to test completion AND odometer.

Reply: Thank you for your comments. We have modified our text as advised (Page 9, lines 141-147).

Feasibility test:

please specify the "distilled solution" used

Reply: Thank you for your comments. "Distilled solution" is sterile saline. We have modified our text on Page 9, line 152.

How was feasibility determined. There was also probably a subjective component about how the physician felt the surgery went, and you should also add a section on this if possible.

Reply: Thank you for your comments. We have supplemented the detailed assessment methods in page 9, lines 154-157.

Results:

The odometer test did not show much difference, which in some ways is surprising and not the case in other similar trials. Where there wide differences between individuals test subjects in each group, and again was there any learning curve.

Reply: Thank you for your comments. In the robot-assisted groups, the participants could control the manipulator with the robot controller instead of manual operation. We considered that the instrument odometer mainly depended on the participants rather than the operation approach. The statistician advised us to use the trim mean calculation method which was accords with the design of this study (Page 10, lines 163-165). Thus, we didn't provide lesrning curve. We added the detailed results of test completion time, odometer, operation accuracy and tremor control (Table 2).

Can you also present the results in tabular form for time, odometer, etc as standardized effect size, SD and confidence interval. Individual data on each subject (in an addendum) might allow researchers in the field to better assess the data.

Reply: Thank you for your comments. We have supplemented table 2 to present the detailed results of test completion time, odometer, operation accuracy and tremor control.

Discussion:

the virtual RCM is an interesting concept. This can also be seen as a co-assistive device that limits certain movements. How did the surgeons fell about the use of the robotic system? did you have any subjective evaluation?

Reply: Thank you for your comments. Your constructive comments have a great impact

on our following study. Other similar trials used questionnaires to compare the participant's impressions of the robot-assisted operation. However, this study aimed to compare robot-assisted vitreoretinal surgery with manual surgery in different preclinical settings, including a simulated setting and an animal model. Thus, we didn't evaluate the surgeons' subjective feelings in this study. Further study may focus on this issue.

Line 258: what is meant by balance?

Reply: Thank you for your comments. "To balance accuracy and efficiency" means that we considered both accuracy and efficiency of robot operation. We have modified our text on page 14, line 269.

Specific comments:

Line 31: please specify that you used donor pig eyes rather than to say microcannulation in an animal model. You can and should be more specific.

Reply: Thank you for your comments. We have modified our text on page 2, lines 30, 34 and 37, page 6, line 83, page 9, line 148 and page 11, line 200.

Line 61: rather than applied use the verb "evaluated"

Reply: Thank you for your comments. we have modified our text as advised (Page 5, line 64).

Line 147: Each participant performed surgery three times (rather than underwent [at least I hope not!])

Reply: Thank you for your comments. we have modified our text as advised (Page 8, line 147).