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Implementing new surgical instruments in minimally invasive surgery

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Human cadavers to evaluate prototypes of minimally invasive surgical instruments: a feasibility study

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Abstract

Background: New technology should be extensively tested before it is tried on patients. Unfortunately representative models are lacking. In theory, fresh frozen human cadavers are excellent models.

Objective: To identify strengths and weaknesses of fresh frozen human cadavers as research models for new technology prior to implementation in gynecological surgery.

Methods: During pre-clinical validation studies regarding the MobiSep uterine manipulator, test procedures were performed on fresh frozen cadavers. Both the experimental setup as the performance of the prototype were assessed.

Results: Five tests including six human cadavers were performed. Major changes were made to the MobiSep prototype design. The cadavers of two tests closely resembled surgical experiences as found in live patients. The anatomy of 4 of the 6 cadavers was not fully representative due to atrophy of the internal genitalia caused by age and due to the presence of pathology such extensive tumorous tissue.

Conclusion: The cadaver tests provided vital information regarding design and functionality, that failed to emerge during the in-vitro testing. However, experiments are subject to anatomical uncertainties or restrictions. Consequently, the suitability of a cadaver should be carefully assessed before it is used for testing new technology.

Introduction

Innovations in surgical instruments and techniques (hereafter called 'technology') are important tools to enhance patient safety in minimally invasive surgery (MIS). They facilitate technically challenging procedures, which constitute MIS. At the same time, experiences in the past have demonstrated the risks that accompany the implementation of such innovations. For instance, the introduction of laparoscopic cholecystectomy resulted in a significant increase of the number of bile duct injuries. In gynecology, prolapse repair surgery using vaginal meshes, Essure sterilization and the use of power morcellators in laparoscopic hysterectomy or myomectomy, are examples of widely used technology that have recently come under scrutiny due to unforeseen adverse effects.[1-4] To reduce the risk of these adverse effects, pre-market approval for new technology by a Conformité Européenne (CE) mark or review by the U.S. Food and Drug Administration (FDA) is required in Europe and the USA respectively.[5] However approval or clearance does not guarantee safety, and even minor changes or additions to an existing technology, which undergo less extensive evaluation, may be hazardous.[6] At present, there are 5 stages in the implementation of new technology into early daily practice [7]: innovation (stage 0), testing of proof of concept and safety (stage 1), development and exploration (stage 2a-b), assessment (stage 3) and long term implementation and monitoring (stage 4). As soon as stage 1, testing is performed on live humans. It is only in stage 0 that the pre-human tests take place. Evidently, compared to the introduction of new pharmaceuticals, which is bound by vigorous protocols, new technology is subject to less strict implementation criteria. This has recently been recognised by the European Parliament (EP). In May 2016, the EP reached a provisional agreement on more strict rules for new technology. In addition, the importance of pre-human stage 0 testing has been incorporated in recent guidelines regarding the introduction of new technology, created by clinicians.[8] These guidelines strongly advise the surgeon to familiarize him- or herself with the new technology by practicing on appropriate training models, before it is implemented in daily practice.[8] However, finding a proper model is difficult. For instance in gynecology, animal models are generally not representative due to different anatomy of the internal genitalia. In addition, virtual reality tools have difficulty depicting real life conditions including tactile feedback.

In theory, human cadavers could be of value in establishing the feasibility and safety of a new product. They are widely used in universities to demonstrate anatomy to medical students. Furthermore, human cadavers have been proposed for the laparoscopic training of residents.[9,10] However, no evidence is available on the use of human cadavers for testing new technology. The aim of our study is to evaluate the strengths and shortcomings of human cadavers as a model for testing new technology in minimally invasive surgery, during the pre-clinical stage of development.

Materials & Methods

Fresh frozen cadavers were used to maximally approach conditions as found in live patients, such as tissue resistance and tissue colour. On arrival at the anatomy department, the cadaver is cooled at -40°Celsius, after which it is stored at -20°C. Before use, the cadaver is defrosted and after use it is stored again at -20°C. It is possible to use the cadaver up to 3 times with this protocol.

To assess the feasibility of fresh frozen cadavers as a model during preclinical testing, the mode of action of a new instrument, the MobiSep uterus manipulator and separator, was tested during a total laparoscopic hysterectomy (TLH) as part of the pre-clinical development stage. The MobiSep instrument consists of a uterine manipulator and a vaginal blade that allows a vaginal approach to colpotomy during hysterectomy (figure 1) .[11-13]

All procedures were performed according to a strict study protocol. The following parameters were rated poor, moderate, sufficient or excellent: accessibility of the vagina, visualisation of the cervix, ease of cervical dilatation, insertion of the manipulator into the cervix, insertion of the intra-uterine tip into the uterus, the ease of manipulation of the uterus and of colpotomy. Furthermore, adverse tissue effects were registered. Standard instruments for MIS were used. The degree of possible manipulation of the uterus was verified by using an existing uterine manipulator (model Vectec®), before the MobiSep instrument was tested.

Experiments were performed at the anatomical laboratories of the University Medical Centre of Utrecht and the Radboud University Medical Centre, Nijmegen. FWJ, JPR and TEN performed all tests. Approval was obtained from the Department of Anatomy of the participating institutes.

Results

Five tests including 6 fresh frozen human cadavers were performed, the results are presented in table 1.

The first hysterectomy was performed abdominally to familiarize the research team with the MobiSep instrument, all other procedures were performed via standard multiport abdominal laparoscopy. The first test was performed using the original MobiSep prototype (figure 1). This device comprises an intra-uterine tip and cervical cup which are attached to a rotational mechanism responsible for uterine manipulation. The

Table 1: test results

		Accessibility of the vagina	Visualisation of the cervix	Cervical dilatation	Insertion of manipulator	Positioning the intra-uterine tip	manipulation	colpotomy	Main instrument adjustments
Test 1		Good	good	poor [a]	Poor [a]	Poor [a]	Excellent	Not performed	Reducing maximal manipulation
Test 2		Moderate	Moderate	Poor [a]	Poor [a]	Poor [a]	Excellent	Not performed	Replacing rotation with DEAM. Independent movement of cervical cup
Test 3		Moderate	Moderate	Moderate	Moderate	Good	Excellent	Poor	Removal of colpotomy function
	Cadaver 1[b]	Moderate	Poor	n/a	n/a	n/a	n/a	n/a	n/a
Test 4	Cadaver 2 [b]	Good	Good	Moderate	Moderate	n/a	n/a	n/a	n/a
Test 5		Good	Good	Good	Good	Good	Good[c]	n/a	Strengthening DEAM

[a] Due to severe atrophy of the internal genitalia

[b] Test 4 could not be performed fully due to the apparent absence of cervix and uterus in one case, and due to a malignancy occupying the small pelvis in the second case.

[c] After cutting uterine ligaments

n/a: not applicable

Fig. 1: MobiSep

Fig. 2: MobiSep

blade to perform colpotomy is located inside the cervical cup. Manipulation up to 90° anteriorly and laterally was demonstrated with MobiSep. However, the extreme range of motion combined with the size of the rotational unit, caused extensive tissue damage, to the point of tearing the uterus from the vaginal wall. Furthermore, due to the design, manipulation posteriorly was not possible.

Based on these results, the prototype was adapted for the second test. The maximum anterior motion was reduced to 60°, and posterior manipulation was added. Furthermore the cogwheel of the rotational unit was encased to prevent tissue damage. Manipulation to the maximum ability of the instrument was feasible. Unfortunately, extensive tissue damage occurred again, this time due to the fixated cervical cup which did not allow adapting to the present anatomy. It was concluded that to avoid tissue damage, the cervical cup and rotational unit should operate separate from each other. However due to the nature of the design, this functionality could not be incorporated into the device. Therefore, the MobiSep instrument was redesigned. The rotational unit was replaced by a

multi-directional intra-uterine tip based on the DEAM mechanism.[14] This mechanism consists of an easy steerable tip and was inspired by the tentacles of a squid. In addition, the new prototype enables independent movement of the cervical cup encasing the colpotomy blade. (figure 2) This blade was first evaluated in test 3. Two issues were found. Firstly, it proved difficult to bring the tissue under sufficient tension with the cervical cup, and to perform the colpotomy in the desired tissue plane and direction. Additional handling of the tissue by the surgeon or the assistant via laparoscopy was needed. Secondly, it was concluded that a thermal or ultrasonic cutting device is preferred over a cold-knife. Due to the complexity of such a system, it was decided to develop a uterine manipulator without separator based on the DEAM system and, parallel to this process, to evaluate the feasibility of a thermal or ultrasonic blade. Test 4 was scheduled to assess the strength of the DEAM system, as originally, this system was developed for endovascular procedures. Although 2 cadavers were available, unfortunately test 4 could not be performed due to anatomical abnormalities of the cadavers. Therefore, a 5th test was organized. Manipulation before the main ligaments of the uterus were dissected proved difficult due to lack of strength of the DEAM system. However, after dissection and before colpotomy, uterine manipulation was excellent in any direction without restrictions. It was the conclusion that the DEAM mechanism has excellent potential as a uterine manipulator, however the strength of this mechanism needs to be further enhanced.

Discussion

The present study describes our experiences with human cadavers as a model for testing the feasibility and safety of new technology in a pre-clinical stage of development. Several strengths of the model were found. The mode of action of the MobiSep device was extensively tested on in-vitro models, where the functionality of all features was established including the rotational mechanism and the vaginal colpotomy blade. Nevertheless, the cadaver tests provided vital information regarding design and functionality of the MobiSep prototype, that failed to emerge during the in-vitro testing. This resulted in a substantial alteration of the MobiSep design and function. The rotational device was removed and replaced by an alternative mechanism, the cervical cup was redesigned to move independently, and the colpotomy blade is further developed before additional testing. Apparently, there is a big gap between results obtained from in-vitro situations versus real life ones. Therefore, it can be concluded that human cadavers as a model offer a valuable contribution in the pre-clinical stage of the development of new technology.

These findings are in agreement with multiple studies demonstrating the benefits of using human cadavers for surgical training purposes. [15-17] Moreover, cadavers as a

laparoscopic training model were preferred over high-fidelity virtual reality simulators. [18] Fresh frozen cadavers were favoured in most studies, although other preservation methods may closely mimic tissue appearance and handling of fresh frozen specimens. [17,19] Interestingly, studies on the value of human cadavers in the developmental stages of new technology were not found.

Our tests also revealed several limitations of the human cadaver model. Only 2 cadavers were regarded as an optimal model (test 3 and 5). The cervix and uterus of the cadavers used in test 1 and 2 were severely atrophied. Cervical dilatation and insertion of the instrument was difficult, even with the standard manipulator. This could have negatively influenced tissue handling and manipulation, which complicates the interpretation of the test results. Test 4 could not be performed altogether, even though 2 cadavers were available. In the first cadaver, a cervix and uterus could hardly be identified, possibly due to a congenital abnormality. The second cadaver apparently suffered from a malignant process spreading throughout the small pelvis. As a result, the bladder, uterus and intestines were incorporated in this process and fixed to the pelvic wall. Therefore, identification of the pelvic organs was not possible and manipulation could not be evaluated.

These limitations could possibly be overcome if more information on the cadaver is available. Privacy legislation however, prohibits the disclosure of the cadavers' full medical history. In addition, the actual anatomy can only be assessed after the cadaver has already been prepared for the test. Finally, not all institutes may have sufficient suitable fresh frozen specimens at their disposal, making it difficult to implement this model on a wider scale.

In addition to this limitations, a critical evaluation is fair from an ethical point of view, regarding the necessity of using human cadavers for testing new technology. In our opinion, the acquired knowledge regarding the mechanism of vaginal colpotomy by the device could only have come from the human cadaver model due to its specific anatomy. Moreover, testing high risk, new technology on cadavers before it is introduced in live patients can easily be justified. However, the results from our study show that a thorough preparation is necessary to select a suitable cadaver for the intended test. Furthermore, considerations in the early stage of development regarding basic design and mode of action, such as instrument dimensions in our case, should ideally be evaluated in proper non-human models. In this light, the ongoing developments in 3D printing are of interest. Recent papers have studied the value of 3D models for training purposes, and the feasibility of creating representative models of human anatomy has been demonstrated. [20-22] These models of human anatomy may prove valuable in the future.

Finally it is important to realise that a cadaver test is one component of the developmental and implementation stage of new technology. In order to minimize the chance of direct or long-term adverse events occurring, several other measurements should be taken. For instance, a prospective risk inventory (PRI) may be attempted, to identify and correct all possible adverse effects before new technology is introduced. [23] In addition, post-market surveillance to register all complications should be centralised and be mandatory.

In all, human cadavers provide important insights of new technology during the pre-clinical developmental stage, before the new technology is tested in live patients for the first time. A thorough preparation to select a suitable cadaver to match the intended test is necessary. This will prevent the improper use of human remains and will ensure that hazards that may be overlooked in non-human models become apparent before tests in live patients.

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