

# Surgical innovation: the ethical agenda

## A systematic review

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### Abstract

The aim of the present article was to systematically review the ethics of surgical innovation and introduce the components of the learning health care system to guide future research and debate on surgical innovation.

Although the call for evidence-based practice in surgery is increasingly high on the agenda, most surgeons feel that the format of the randomized controlled trial is not suitable for surgery. Innovation in surgery has aspects of, but should be distinguished from both research and clinical care and raises its own ethical challenges.

To answer the question “What are the main ethical aspects of surgical innovation?”, we systematically searched PubMed and Embase. Papers expressing an opinion, point of view, or position were included, that is, normative ethical papers.

We included 59 studies discussing ethical aspects of surgical innovation. These studies discussed 4 major themes: oversight, informed consent, learning curve, and vulnerable patient groups. Although all papers addressed the ethical challenges raised by surgical innovation, surgeons hold no uniform view of surgical innovation, and there is no agreement on the distinction between innovation and research. Even though most agree to some sort of oversight, they offer different alternatives ranging from the formation of new surgical innovation committees to establishing national registries. Most agree that informed consent is necessary for innovative procedures and that surgeons should be adequately trained to assure their competence to tackle the learning curve problem. All papers agree that in case of vulnerable patients, alternatives must be found for the informed consent procedure.

We suggest that the concept of the learning health care system might provide guidance for thinking about surgical innovation. The underlying rationale of the learning health care system is to improve the quality of health care by embedding research within clinical care. Two aspects of a learning health care system might particularly enrich the necessary future discussion on surgical innovation: integration of research and practice and a moral emphasis on “learning activities.” Future research should evaluate whether the learning health care system and its adjacent moral framework provides ethical guidance for evidence-based surgery.

**Abbreviations:** IRB = institutional review board, LHS = learning health care system, RCT = randomized controlled trial.

**Keywords:** ethics, learning health care system, surgical innovation

### 1. Introduction

Rising health care costs and subsequent scarcity in health care, as well as recent controversies involving innovative surgical procedures, elicited debate on the ethics of surgical innovation. Although the call for evidence-based practice in surgery is increasingly high on the agenda, innovation in surgery often takes place outside controlled study conditions. After all, in most parts

of the world, the clinical introduction of surgical techniques and sometimes also novel medical implants occurs with relatively little oversight and regulation. This is in contrast to strong regulatory and ethical requirements for the introduction of novel pharmaceuticals. There is increasing consensus that not only new drugs, but also novel surgical interventions should be properly assessed.

In general, the randomized controlled trial (RCT) is considered the most rigorous form of research. However, most surgeons feel that the format of this form of research suffers from various limitations including the felt lack of equipoise, and ethical problems related to the double-blinded design with sham surgery as a potential control.<sup>[1,2]</sup> Because of these limitations and the strict format of the RCT, surgeons have been reluctant to set up surgical trials, also because other trial formats may be more suitable. This is also defended or explained by “surgical exceptionalism,” the view that the somewhat exceptional ethical or regulatory status of surgery is justified by the unique nature of surgery.<sup>[3]</sup> There are several reasons why surgeons have taken this view, for example, because the results of surgical techniques are more difficult to measure than drugs, because surgical procedures are more difficult to reproduce than drugs, or because the strict paradigm of oversight and systematic research in drugs should not be applied to surgery for it would stifle innovation.<sup>[4]</sup>

Surgical innovation and research have indeed been shown to differ in several respects. First, the primary goal of innovation is

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often care and not to generate generalizable knowledge. This is illustrated by a recent case of a young patient who suffered from increased intracranial pressure due to the rare Van Buchem disease leading to thickening of the skull, who received a complete 3D printed technology skull. In a case like this, where not to operate would inevitably result in neurological deterioration and eventually the death of the patient, providing her with a “new” skull seemed one of the only possible medical interventions. This was to our knowledge (one of) the first complete 3D printed skull(s) that was implanted, and the primary goal of this innovative procedure was clinical care. As such, contrary to what would have been the procedure for research, no research protocol had been submitted before the implantation and no institutional review board (IRB) approval was sought. Besides, it is questionable whether setting up a trial for 3D printed technology skull would even have been possible, and if a trial would have been conducted, what the correct control would have been as sham surgery in a case like this is not only ethically unacceptable but also practically impossible.<sup>[5]</sup>

In many surgical specialties, populations are often small, which makes outcomes rarely statistically significant, and double-blinded surgery is simply not possible. In a case like this, it is unclear what precautions should be met before the surgery and, in case a proposal would have been submitted, whether the innovation proposal should be reviewed by some sort of ethics committee. Innovative procedures are not without risks, and knowledge of guidelines for surgical innovation to ensure patients’ safety is currently lacking. To gain more insight in the ethical questions related to surgical innovation, we systematically reviewed the literature on the ethics of surgical innovation. In this article, we first identify the main ethical aspects of surgical innovation as presented in the literature. We will subsequently put forward 2 aspects of a so-called learning health care system that might enrich the necessary future discussion on surgical innovation.

## 2. Methods

After identifying our research question: “what are the main ethical aspects of surgical innovation?”, we (MEC and MLDB) systematically searched PubMed, and Embase on July 4, 2015, for papers on the ethics of surgical innovation using the following electronic search strategies in PubMed: (“Morals”[Mesh] OR “Ethics”[Mesh] OR “Ethics, Medical”[Mesh] OR “ethics”[Subheading] OR ethical[Title/Abstract] OR ethics[Title/Abstract] OR moral\*[Title/Abstract]) AND (innovat\*[Title/Abstract] OR invent\*[Title/Abstract] OR renewal\*[Title/Abstract]) AND (“Surgical Procedures, Operative”[Mesh] OR surgery[subheading] OR surgical[Title/Abstract] OR surgery[Title/Abstract] OR surgeries[Title/Abstract] OR procedur\*[Title/Abstract] OR operation\*[Title/Abstract]) and in Embase (‘morality’/exp OR ‘ethics’/exp OR ‘medical ethics’/exp OR ethical:ab,ti OR moral:ab,ti OR ethics:ab,ti) AND (innovat\*:ab,ti OR invent\*:ab,ti OR renewal\*:ab,ti) AND (‘surgery’/exp OR ‘surgical technique’/exp OR surgical:ab,ti OR surgery:ab,ti OR surgeries:ab,ti OR procedur\*:ab,ti OR operation\*:ab,ti), supplemented by hand searching of the bibliographies of the papers retrieved by the electronic search. This review is restricted to published data. Only papers written in English, Dutch, French, or German were considered for this review. The search was not limited by date of publication.

Titles and abstracts of retrieved citations were screened, and potentially suitable studies were read in full by all authors. As we

are interested in what in the literature is presented as the ethical challenges of surgical innovation, only papers expressing an opinion, point of view, or position were included, that is, normative ethical papers. Review papers were used to check whether any underlying arguments were missing, which was not the case. (Supplementary Fig. 1, <http://links.lww.com/MD/B50>) Data on year of publication, type of article, level of evidence, and studied ethical theme, and recommendations, were extracted by the authors. Disagreements were solved by discussion.

## 3. Results

We included 59 studies discussing ethical aspects of surgical innovation. These studies discussed 4 major themes: oversight, informed consent, learning curve, and vulnerable patient groups.

### 3.1. Oversight

Thirty-one papers discussed oversight for surgical innovation.<sup>[6–36]</sup> The IDEAL Collaboration developed a framework for surgical innovation, describing 5 phases (stage 1–4) of development.<sup>[6]</sup> In the first phase, when a new procedure is tried first-in-man, the innovator should have informed the hospital of his plans in prospect, but no research ethics approval would be necessary. Next, in the development phase, when the procedure is tested in a small group of patients to assess its efficacy, prior ethical approval must be given.<sup>[6,7]</sup>

In the literature, we found that formation of a new “innovations committee” to manage this kind of innovation has been suggested by some. However, authors disagree on the format and tasks of such a committee.<sup>[8–12,14–18]</sup> For instance, McKneally et al<sup>[10]</sup> suggested back in 1999 that a regional board for innovations should be established rather than a single IRB, with members including practitioners, potential patients, payers, and institutional representatives. Their tasks should include planning, evaluation of ongoing activities, assessment of endpoints and outcomes, and public reporting as well as review of proposed treatments.<sup>[10]</sup>

Morreim et al<sup>[9]</sup> suggest the establishment of a committee in the institution where the innovation takes place, with members from that institution with the necessary expertise. This committee should study before the start of the novel treatment several aspects, including but not limited to the necessity for introduction of a novel intervention, the performed laboratory studies, criteria for patient selection, and management of surgeons’ learning curves. Moreover, the committee should retrospectively look at how well the realities matched the hopes, any unanticipated problems, and whether the innovation requires additional studies.<sup>[9]</sup> Others have argued that the national societies should play an important role in the oversight and regulation of innovation in surgery.<sup>[13,29,30]</sup>

It has also been suggested that oversight for surgical innovation depends on the type of innovation. However, a recent study showing the results of interviews with 18 surgeons on what is innovation, showed that (the interviewed) surgeons hold no uniform view of surgical innovation, and that there is no agreement on the distinction between innovation and research.<sup>[19]</sup>

In the literature, 3 types of innovation can be distinguished: minor modifications of a standard procedure; major modifications of an established technique or radically new innovations; and innovations that are new to the institution, but have been validated elsewhere.

With regard to the first category, some authors suggest that certain forms of surgery, for example, minor modifications of an existing technique, do not require oversight.<sup>[35]</sup> Others argue that also this kind of innovation needs some form of oversight. This review could be done by peers, a group of interested surgeons, by the surgeon-in-chief, and/or by an IRB.<sup>[8,21,22,31,32,35,36]</sup>

With regard to the second category, most authors suggest some form of formal review. This formal review could be done by the IRB, possibly after endorsement of the procedure by senior peers and the chief of surgery, or by an external institution. Some authors propose a surgical review committee organized on a national level.<sup>[15,22,23,29,31]</sup>

With regard to the third category, several routes are suggested, ranging from consultation of the surgeon-in-chief to peer review, IRB approval, and the establishment of an RCT.<sup>[15,23–25]</sup>

Many argue that oversight should not only focus on the potential threats to patients, but also on identification of potential conflicts of interest and costs.<sup>[26–28,33,34]</sup>

### 3.2. Informed consent

Thirty-six papers address several aspects of informed consent. They either describe what information to patients undergoing innovative procedures is needed for informed consent or how informed consent should be obtained.<sup>[8,11,14–17,20,22,24,26,27,32,34,37–59]</sup> Information that should be provided includes the following interrelated elements: the innovative nature of the procedure<sup>[8,11,14–16,34,37–49]</sup>; the corollary surgeon's learning curve, referring to his experience with the procedure<sup>[20,22,24,37,49–52]</sup>; the risks and benefits of the procedure<sup>[8,15,17,20,26,27,34,37,39,41,43–47,53,54,59]</sup>—possible, unforeseeable or unknown risks, or outcomes should be discussed likewise because of the experimental and invalidated nature of the procedure<sup>[22,41]</sup>; the evidence, or lack thereof<sup>[11,20,22,44,48,55]</sup>; alternatives to the innovative procedure.<sup>[8,15–17,26,27,38,41,42,44,46,47,54]</sup> Strikingly, whereas a small majority of patients seem to consider the technical details of the operation as essential information to decide on having an innovative operation, only 20% of the surgeons think this should be the case.<sup>[45]</sup>

Several groups described the format of the informed consent procedure. Suggestions included a third party communicator when the researcher is the physician or when for other reasons extra help is needed,<sup>[37,14]</sup> consultation of a patient advocate,<sup>[34,56]</sup> and the addition of a multimedia presentation to explain the procedure to the patient.<sup>[57,58]</sup>

### 3.3. Learning curve

Fourteen papers discussed the surgeon's learning curve.<sup>[7–9,11,12,21,22,24,26,34,37,39,44,53]</sup> Most authors agree that some form of training for surgeons performing novel procedures is necessary. Examples of how to deal with the surgeon's learning curve include hands-on training (in animal models or human cadavers),<sup>[8,24,26,39]</sup> visiting different surgeons who are performing the procedure,<sup>[12,22]</sup> and the presence of a mentor or even a committee.<sup>[11,21,24,26]</sup> Experience and outcomes should be shared with peers.<sup>[8,12,37,44]</sup>

Some authors suggest a system of accreditation for performing a novel procedure.<sup>[7,9,22,34,39,53]</sup> This means that with the introduction of a new surgical technique, surgeons will be trained, credentialed, and monitored.

### 3.4. Innovative procedures in vulnerable patients

Six papers discussed innovative procedures in vulnerable patients such as unconscious patients, patients in emergency situations, disease refractory patients, and children.<sup>[18,32,60–63]</sup> They agree that in case of vulnerable patients, alternatives must be found for the informed consent procedure.<sup>[18,32,60–63]</sup> For instance, in emergency situations and unconscious patients, some suggest that when possible, waivers must be obtained from an IRB before using the innovative procedure.<sup>[32,60]</sup> Alternatively, in an emergency situation the family or guardian should consent to the procedure.<sup>[61]</sup> In some emergency situations, it might be necessary and justifiable to even refrain from obtaining informed consent.<sup>[32]</sup>

Vulnerable patients, for example, brain tumor patients who might easily consent to any alternative, innovative, procedure in face of the approaching end of life, should be well informed and some authors suggest seeking a second opinion of an independent surgeon.<sup>[61]</sup>

Innovative procedures in children require informed consent not only from their parents, but also from the patients themselves.<sup>[62,63]</sup>

## 4. Discussion: toward a learning health care system?

The reviewed studies on the ethics of surgical innovation discussed 4 major themes: oversight, informed consent, learning curve, and vulnerable patient groups. Although all papers addressed the ethical challenges raised by surgical innovation, surgeons hold no uniform view of surgical innovation, and there is no agreement on the distinction between innovation and research. Some groups try to come up with a workable classification of procedures, for example, Schwartz who divides procedures in practice variation, experimental research, and procedures in a so-called “transition zone.”<sup>[18]</sup> The Society of University Surgeons aims to clarify the difference between “variations” (minor modifications not requiring specific disclosure), “innovations” (modifications of potential significance to the patient, requiring disclosure), and “research” (systematic investigations designed to develop or contribute to generalizable knowledge).<sup>[15]</sup> However, most papers did not provide an explicit definition of what should be considered surgical innovation. This difficulty defining surgical innovation was also observed when surgeons were asked to define and identify surgical innovation.<sup>[19]</sup> Clearly, some uniformity on what exactly is surgical innovation is a prerequisite when considering to launch surgical oversight committees. Otherwise it remains ambivalent which kinds of innovation should or should not be submitted for review.

Even though most groups agree to some sort of oversight, they offer different alternatives ranging from the formation of new committees, especially designed for surgical innovations, to establishing national registries. Most groups seem to agree on the fact that informed consent is necessary for innovative procedures and that surgeons should be adequately trained to assure their competence to tackle the learning curve problem. All papers agree that in case of vulnerable patients, alternatives must be found for the informed consent procedure.

Given the importance of these 4 major themes related to surgical innovation, we believe that the lack of oversight and systematic research is no longer defensible. Not only new drugs, but also novel surgical interventions should be properly assessed. However, too stringent RCTs might not be the best format to achieve this<sup>[1,2]</sup> and might even stifle innovation. Therefore, we

applaud that alternatives for the conventional RCT are being explored. Examples of these include feasibility RCTs, expertise-based RCTs, cohort multiple RCTs, step-wedge design studies, and controlled-interrupted time series.<sup>[61]</sup>

Recently, the concept of “learning health care systems (LHS)” was introduced. A learning health care system is defined by the Institute of Medicine as “a health care system in which knowledge generation is so embedded into the core of practice of medicine that it is a natural outgrowth and product of the healthcare delivery process and leads to continual improvement in care.”<sup>[64]</sup> The underlying rationale of the learning health care system is to improve the quality of health care by embedding research within clinical care. In a learning health care system, continuous monitoring could detect suboptimal care or uncertainty with routinely used interventions. It follows what has so been called a “test, learn, adapt” methodology which focus on continuous learning and improving.<sup>[65]</sup> Two aspects of a learning health care system might enrich the discussion on surgical innovation.

First, whereas the dominant paradigm in research ethics and regulation has departed from a sharp distinction between research and care, learning health care systems have an oversight that is commensurate with risk and burden in both realms. For surgical innovations this would mean that these do not need to be categorized as either a research or care activity, but need to be viewed in light of the added risks and burdens to patients. Is the innovation first-in-man, first-in-a-country, or only first-in-hospital? Depending on the level of risk and the experience of the medical team, oversight would be put in place in an LHS.

Second, the moral emphasis in the learning health care system is put on “learning activities.”<sup>[66]</sup> Whereas the RCT is perceived as the standard format for generating new knowledge, there may be other ways of learning and generating knowledge, particularly in surgery. Examples include the establishment of registries, and sharing experiences including complications. The large-scale registration is still in its infancy in surgery. Moreover, in surgery, “hazardous” attitudes are reported such as impulsive behavior, macho, and invulnerable behavior.<sup>[67]</sup> This is rather opposite to the characteristics of a learning health care system, which requires self-reflection, vulnerability, and the willingness to change. Therefore, if the learning health care system is considered a suitable model for surgical innovation, a novel professional attitude in surgery is required, focused on continuous learning.

## 5. Conclusions

The literature on the ethics of surgical innovation highlights 4 themes: oversight, informed consent, learning curve, and vulnerable populations. As innovation in surgery has aspects of, but should be distinguished from, both research and clinical care, these themes require further scrutiny in light of the special nature of surgical innovation. We contend that the lack of oversight and systematic research is no longer defensible, but we caution against rushing into the evidence-based medicine paradigm without taking into account the special situation and characteristics of surgical innovation. Future research should evaluate whether the learning health care system and its adjacent moral framework provides ethical guidance for evidence-based surgery. We applaud an emphasis on continuous “learning” in surgery, for example, by setting up more structured research and registries to create a surgical practice that continuously improves care by learning from available data. An environment where learning is perceived as an ethical imperative requires a culture characterized

by self-reflection, vulnerability, and the willingness to change. We therefore make an appeal to the surgical profession to examine and implement the cultural change necessary to build a learning surgical practice.

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