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Review

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Surgical data processing for smart intraoperative assistance systems

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Abstract: Different components of the newly defined field of surgical data science have been under research at our groups for more than a decade now. In this paper, we describe our sensor-driven approaches to workflow recognition without the need for explicit models, and our current aim is to apply this knowledge to enable context-aware surgical assistance systems, such as a unified surgical display and robotic assistance systems. The methods we evaluated over time include dynamic time warping, hidden Markov models, random forests, and recently deep neural networks, specifically convolutional neural networks.

Keywords: surgical process modeling; surgical robotics; surgical user interface; surgical workflow analysis.

Introduction

Surgical data science recently developed as a new interdisciplinary research field between medicine, computer science, and engineering. Some of the major components of this field, referred to as surgical workflow analysis or surgical process modeling, have been the focus of research conducted by several international groups for more than a decade now. Here, we provide an overview of the research done in this field by our groups and some of its target applications we are currently working on. The focus is laid on the integration of mechatronic platforms into the overall workflow as an integrative part of the cooperative surgical environment.

The term "surgical data science" covers many goals and applications based on the definition developed at a joint workshop [1], including intraoperative decision support and surgeon training in a very general sense. Our focus in this field, however, lies in the monitoring, analysis, and recognition of the surgical workflow to provide context-aware assistance by various support systems, including mechatronic platforms such as surgical robots.

Various groups are working on developing and formalizing surgery models automatically from individual, recorded procedures [2, 3]. Many try to detect surgical gestures [4, 5], activities, or phases [6–8] directly from available data without the usage of models. A review on this topic is available from Lalys and Jannin [9].

In this article, we first briefly present the different techniques proposed by our own groups and a short summary of their respective experimental results and possible applications. Based on these, we describe in detail an additional new application field of workflow analysis and prediction in the surgical operating room (OR). Beyond automatic situation understanding, objective performance evaluation, and context-aware intraoperative visualization, the integration of robotic assistance systems is delineated. Finally, we discuss the possibilities of a fully workflow-enabled, context-aware OR of the future.

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Workflow detection techniques

As one of the first groups to do this, we avoided using predefined surgical models and aimed rather at modeling and monitoring the surgical workflow only based on acquired sensor data [10]. Several methods have been applied to this end, from dynamic programming more than a decade ago to advanced machine learning in the recent years, as will be explained in the following sections.

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Dynamic time warping (DTW)

DTW can be used to synchronize two separate but similar time series and has originally been developed for speech recognition [11, 12]. To compare different laparoscopic cholecystectomies, we recorded simplistic, binary usage data of surgical tools in Ref. [10]. For every time step (in this case with a resolution of 1 min), the status of 17 different laparoscopic tools was stored in a multidimensional instrument vector as 1 if the tool was in use and as 0 otherwise (see Figures 1 and 2). The resulting signals included some with a very low rate of change, such as the one representing the presence of trocar ports placed in the beginning of the surgery and removed only at the end, as well as frequently changing ones, such as the status of the monopolar cutting or coagulation current.

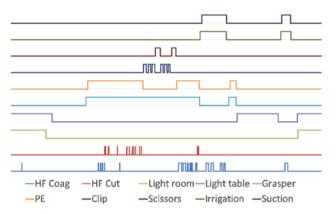


Figure 1: Exemplary, ideal instrument usage signals used for workflow recognition.

Each line represents a single signal that is active if the line is at the top and inactive otherwise.

These recorded surgeries could now be synchronized pairwise to each other using DTW. By choosing a single surgery arbitrarily as temporary reference, we can synchronize all other surgeries to the reference recording, exploiting the transitivity of DTW. The obtained warp paths can be interpolated and averaged to create a warping path between the reference and a virtual, average surgery. By applying the inverse of the common warp path to the timing of the synchronized surgeries first, each recorded surgery can be warped to match the timing of the virtual surgery. Then, the average surgical model can be calculated by averaging the warped instrument vectors. The binary usage data of each tool changes due to the averaging to an approximation of the probability that the tool is being used at this point of time during the surgery.

Labeling the average surgery provides a baseline for workflow detection very similar to an anatomical atlas for organ and structure segmentation. Newly recorded surgeries can be mapped to the average surgery, after which the labels of the average surgery can be applied to the corresponding times of the tested surgery. When comparing the mapped phase boundaries to known ground-truth annotations 92% of all events were correctly identified with a tolerance of 5 s and 83% even with a tolerance of 1 s.

Hidden Markov models (HMM)

HMMs also originated from the field of speech recognition [13] and can model sequences of observations into a traversal of a graph of hidden states automatically. For the application in surgical workflow recognition, the observations in each time step correspond to the recorded

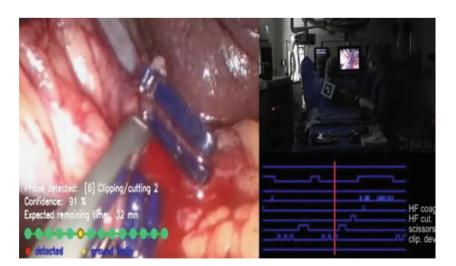


Figure 2: Combined view showing the current laparoscopic view (left), the situation in the OR (top right), and recorded instrument signals (bottom right), with a prediction of the current and upcoming phases (overlay).

instrument vector. Often, the model is trained on the premise of using a single state per expected phase, so that a one-to-one relationship between hidden states and phases can be established, although other approaches exist. HMMs additionally have the advantage over DTW that they can work on partial sequences, so the methods based on HMM have the potential to be applied to a running surgery in real time.

In the work by Padoy et al. [14], a separate HMM was trained for each surgical phase, so that the correct recognition of the overall phases is not negatively influenced by the variability of the performed actions in each phase. These individual models were built with a number of hidden states correlated to the square root of the corresponding mean phase duration. The results of this experiment were also compared to HMM built by forcing only a single or two states per phase each. The overall detection accuracy over all phases was 92.4% for the dynamic model, whereas the static models with one or two states per phase reached 84.2% and 87.4%, respectively.

Another approach by Blum et al. [15] uses adaptive model merging to reduce the number of states from a single state per sample up to only a single state for the entire surgery. By merging the recordings of multiple different surgeries of the same type, this method can be used to visualize and analyze all variations and bottlenecks encountered in this surgery type. Using a specialized UI, it is possible to freely navigate the model by merging a state with the calculated best merging candidate via clicking or by splitting a merged state into the corresponding source states again. Thereby, a user can focus on specific parts of the surgery while accessing as much details about phases, steps, and gestures as necessary.

Canonical correlation analysis (CCA)

Contrary to the detection of instrument usage, the laparoscopic video is by definition always available during minimally invasive surgeries and usually very easy to obtain. This has been employed in Ref. [16], where many image features have been extracted from the laparoscopic video. This high-dimensional feature space has been mapped to a common, low-dimensional feature space with manually annotated instrument usage data. The obtained mapping is then used to reduce the number of image features to fewer, semantically more meaningful features, which in turn serve as features or observations in DTW or HMM, respectively. The best result of 76.8% accuracy was achieved using DTW on the transformed features.

Random forests

In an approach to automatically detect instrument usage during a surgery (instead of manual annotations), our clinical partners attached radiofrequency identification (RFID) tags to each instrument and an appropriate antenna to the instrument table [17]. The data obtained through this detection, in addition to other sensors to detect intraoperative light status, HF modes, table inclination, intra-abdominal pressure, and the weight of the irrigation and suction bags, were the data basis for the work in Ref. [18]. To robustly handle the heavy noise in the recorded data, the machine learning technique of random forests was used. A forest of 50 randomized decision trees with maximal node depth of 4 was trained to classify each sample into any of the seven possible surgical phases. An average accuracy of 68.8% was achieved directly on the unfiltered sensor data.

A later improvement of the method [19] used the classification output of the random forest as observations for a subsequent HMM. The HMM was trained to represent each surgical phase with a single hidden state. This sequential usage enables the combination of mostly reliable classification of the random forest with the modeling structure of the HMM to produce a relatively stable and smooth classification output. This achieved an accuracy of 80.8% on the unfiltered sensor data and 82.4% when additionally preprocessing the sensor data with noise reducing filters.

Convolutional neural networks (CNN)

Due to the increasing availability of inexpensive highperformance hardware, so-called deep neural networks were widely adopted. Especially, CNNs have become a powerful tool for image understanding, as they can be trained without manual parameter adjustment on very large data sets to obtain highly robust results. Recent works focused so far on detecting straightforward surgical events, such as the presence of blood or smoke (see Figure 3), or detecting and locating surgical tools or anatomical structures in the surgical video, or more abstract workflow information [20].

Future surgical applications

With our background in recognizing and modeling the surgical workflow from simple and easily obtainable sensor data, our vision for surgical data processing in the near future consists of the following four major aspects.



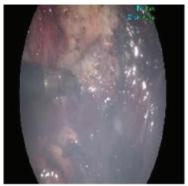




Figure 3: Video frames of an endoscopic surgery, which were correctly classified to contain (A) blood, (B) smoke, or (C) neither by our CNN

The images were preprocessed and rescaled to a square format to be able to use images of varying qualities from different sources with the same classification framework.

Automatic understanding of the surgical situation

Surgical workflow recognition provides the basis for a broader recognition of the surgical context, including the detection of anomalies and emergencies. This constitutes the required infrastructure for any context-sensitive system in the OR of the future. Immediate applications of scene understanding are also possible, for example, in the form of the automatic generation of surgical reports or report templates, in which relevant key events are mentioned and possibly weighted based on the duration spent on related activities.

Objective evaluation and comparison

A long-term goal of surgical data science is also to be able to create completely novel surgical processes enabled by advances in medical devices, imaging, and robotics. Such new processes are challenging to compare manually to existing procedures in a short time frame, so support by workflow analysis is strongly required. The same methods can often also be applied to evaluate the dexterity of young surgeons during their training and help with personalized training support.

An early approach was proposed in [21], where several laparoscopic surgeries were recorded, synchronized through DTW (see "Dynamic time warping" section), and their laparoscopic videos played back in parallel (see Figure 4). This method provided a strong distinction between young and expert surgeons. The activities in which the young surgeons had little to no practical experience could be clearly identified in comparison to the experts, whose synchronized videos were frozen during that time, as they completed the task in a significantly shorter time.

Context-aware intraoperative visualization and control

The goal of many modern integrated OR suites is to provide every needed information to the surgeon. They often accomplish this goal by displaying as much data as possible on large wall- or ceiling-mounted monitors. These setups offload the cognitive task of filtering the data for useful information completely to the surgeon. They also usually tend to be rather large, which prevents them from being close to the patient and surgeons, so it is impossible to use them interactively. More practical, small, single-display solutions have to filter the displayed information. This filtering must happen automatically in order not to burden surgeons with additional user interactions. This requires knowledge of the surgical context. Thus, the detection and prediction of the workflow is imperative for the next generation of intraoperative unified user interfaces (UI).

A prototypical implementation of such a UI has been presented in [22]. A tablet PC was wrapped in sterile foil and placed next to the situs in direct access for the surgeon. Throughout a simulated surgery, based on the detected phase, the display switched between different, available views, showing various sources such as preoperative planning data or intraoperative imaging data. Due to the immediate access of the tablet, it was also possible to provide interactive touch elements to the surgeon, such as buttons or sliders, to trigger events or adjust device parameters.

Medical augmented reality (AR) [23] provides a more direct way of visualizing supportive data, although it is



Figure 4: Six surgical videos synchronized through DTW. The time stamp in each image represents the position in the corresponding source video. The video is paused where the time stamp is shown with blue background to let other videos catch up to the same relative position in the synchronized workflow.

not yet that common due to the high technical complexity and hardware requirements. The goal of medical AR is to display medical imaging data directly in the surgeon's field of view either through AR displays such as headmounted displays or by augmenting common displays with matched overlays. Challenges of this technology are not only the required tracking and alignment precision but also a convincing visualization to avoid problems with depth perception. The advantages of this technology are a more intuitive presentation of medical data and easier correlation between the data and the patient. Additionally, the visualization can be enhanced through simulated tools such as virtual windows or virtual mirrors. The prior knowledge of the surgical workflow is also required for such applications to choose an appropriate visualization style highlighting the most relevant information at each moment of the surgical procedure.

Workflow-based control of robotic assistance systems

Robot-assisted surgery (RAS) is gaining popularity with the increased availability and safety of surgical robots (Figure 5). Currently, all robotic systems in surgery have a strict master-slave relationship, so their movement is controlled exclusively and directly by a surgeon-controlled input device. Although fully autonomous robots are still



Figure 5: Robotic assistance system controlling the laparoscopic camera during an intervention.

far away, it is now at least possible to support the controlling surgeon through gesture completion or responsive controls.

It would be sensible for many reasons to break up the encapsulated systems and to make them communicate with the comprehensive surgical environment. In a master-slave system, a wealth of information is generated when it is being used. The range and quality of information varies with the type of the robot, but all of them are highly valuable for the purpose of workflow analysis (Table 1). With the vast amount of additionally available real-time data, a robotic system can act as "super sensor",

Table 1: Information directly generated by mechatronic support systems, or derived from those, usable for workflow detection.

Kinematics of the actors and camera (Stereoscopic) video images Applied forces
Action currently being performed Operator readiness
Distance measurements Tissue structure

which could be particularly helpful for the machine learning approaches mentioned in the "Dynamic time warping" section. Whereas some of these data can also be acquired by dedicated sensors (e.g. the type of instruments in use), many others can be provided exclusively by the mechatronic support system.

Even more interesting than the role as an additional source of data is to use the robot as an active tool at the service of the workflow analysis and prediction process as shown in Figure 6.

The aim is clear: As soon as the assistance system has become cognitive and context-aware and as soon as it is able to foresee the next actions required, it should be capable to reduce the surgeon's workload by taking over part of the tasks by itself, acting autonomously. From the surgical point of view, this would be highly attractive, offering an opportunity to relieve the surgeon from tedious tasks such as camera readjustment or knot tying. On the contrary, autonomous actions could become extremely hazardous if the machine decides to perform the wrong action, which is by far worse than just remaining passive. Due to the specific conditions, the difficulties in "automated surgery" are in orders of magnitude greater than autonomous car driving and there is a very low probability to overcome them in the near future.

Nonetheless, it appears to be conceivable that at least some segments of the surgical workflow are suitable for

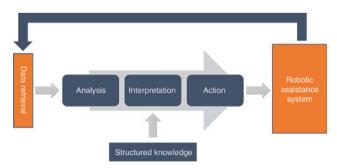


Figure 6: Sequence of data retrieval, analysis and interpretation, and prediction: The robot can provide data in the beginning of this process, but it could also be the active lever at the end of the process to translate the elaborated knowledge about what has to be done next into autonomous actions.

automation (Table 2). These steps or tasks should not be too sensitive to misinterpretation or erroneous, cognitive decisions but rather depend on mechanical and precise manual tasks. The last given example of anastomotic closure is certainly the most elaborate option, as it requires the highest quality in image understanding and force sensing. Although after the initial steps from the surgeon, this task does not involve further decisionmaking, contrary to other aspects of surgery, such as the positions and margins required for cutting around a fumor.

Suturing and knot tying are well-defined sequences of rather uniform motions of the instruments, requiring considerable manual skills, which are tedious and time consuming. A robotic support system should be ideally suited to carry out this procedure, with the surgeon just giving "start" and "stop" commands [24]. In a similar way, the surgeon can define a larger tissue area where the cancer material is expected. A robotic assistance system can then automatically take biopsy samples in a regular grid pattern within that area. This allows for the first time to perform such a meticulous and precise sampling.

If a mechatronic support system provides stereoscopic imaging (as many of them do), continuous real-time distance measurements are a feasible technical challenge for the near future. This could then be used to define virtual working spaces to avoid unwanted collision with sensitive tissue, other instruments, or other artificial conditions of the environment.

A further aspect of surgery that may be performed by robotic systems in the future is the preparation and delivery of tools to the surgeon [25]. This task still has many unsolved challenges, such as the correct identification of tools and safe handover procedures between robot and humans. The knowledge of the current workflow phase can be also used here to predict and prepare the next most likely required tool, which can greatly aid the recognition of spoken requests and reduce prohibitive delays. A subtle understanding of what is actually going on could

 Table 2:
 Surgical tasks potentially apt for autonomous performance.

Camera control Motion compensation Suturing and knot tying Instrument preselection US guidance Instrument and configuration change Lightweight SPECT imaging Emergency instrument withdrawal Avoidance of collision Needle and trocar placement Suction, irrigation, and Large area biopsy sampling in a grid hemostasis Positioning in hybrid Anastomotic closure interventions

even prepare the system for immediate reaction in case of emergency, that is, conversion to open surgery.

In a farther future, robots can also support surgeons by operating other intraoperative imaging sensors, such as ultrasound (US) [26, 27] or SPECT imaging [28, 29]. A lightweight robot with force-sensing joints is capable to move a US probe with perfectly constant speed and pressure over the patient's skin, whereas a robot with gamma cameras is able to scan from locations, which provide the highest gain in tomographic reconstruction based on calculated areas of uncertainty. This increases the repeatability and reliability of the scans already by itself and can replace other, usually rather bulky equipment in the OR. More importantly, however, is the potential of supportive cooperation, as surgeons cannot operate multiple robotic systems themselves at once, especially when performing their own surgical actions. Esposito et al. [29] show that the robot and surgeon can collaborate to perform multimodal US- and gamma-guided needle biopsy. Workflow-aware control and assistance between the different systems and the surgeon is mandatory for this complex level of support.

Discussion

The amount of information available to the surgeon during an intervention has always been growing, and this trend is most likely going to continue in the foreseeable future. However, to prevent disruptive cognitive overload on surgeons in the coming years, the presentation and especially the utilization of relevant data must be improved.

Recently, robotic support systems have also been widely adopted in many hospitals. In the coming decade, the presence of robotic systems is expected to increase, as more procedures will adopt this technology, and novel, truly hybrid surgical procedures can be developed based on robotic support. Such systems could not be efficiently deployed without a complete digital and automatic monitoring of surgical workflow providing the robotic system with additional intelligence in their action and interaction with surgical crew. Surgical robots have a special relevance for surgical data processing, as they both benefit from workflow knowledge, and provide additional sensor, as a result of their accurate kinematic tracking, improving the detection and monitoring of surgical workflow.

In summary, it can be seen that the management of intraoperative data flow is mandatory in modern ORs, with surgical data processing and reliable workflow analysis leading to a prospective judgment on the further workflow. This would enable robots to become cognitive,

cooperative assistants with a major positive impact on the development of surgery. Yet, further research and development on workflow analysis and surgical data processing, as the ones presented in this paper, are absolutely necessary to achieve this goal.

Author Statement

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Author Contributions

Ralf Stauder: Conceptualization; Funding acquisition; Methodology; Software; Writing - original draft. Daniel Ostler: Data curation; Resources. Thomas Vogel: Data curation; Investigation; Validation. Dirk Wilhelm: Data curation; Investigation; Validation. Sebastian Koller: Conceptualization; Funding acquisition; Project administration; Visualization; Writing - review and editing. Michael Kranzfelder: Formal analysis; Investigation; Resources. Nassir Navab: Funding acquisition; Supervision; Writing review and editing.

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Reviewer Assessment

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Reviewers' Comments to Original Submission

Reviewer 1: anonymous

Aug 11, 2017

Reviewer Recommendation Term: Accept with Minor Revision **Overall Reviewer Manuscript Rating: Custom Review Questions** Response 5 - High/Yes Is the subject area appropriate for you? Does the title clearly reflect the paper's content? 5 - High/Yes Does the abstract clearly reflect the paper's content? Do the keywords clearly reflect the paper's content? 5 - High/Yes Does the introduction present the problem clearly? 5 - High/Yes Are the results/conclusions justified? 4 How comprehensive and up-to-date is the subject matter presented? 5 - High/Yes How adequate is the data presentation? 4 5 - High/Yes Are units and terminology used correctly? Is the number of cases adequate? N/A Are the experimental methods/clinical studies adequate? N/A Is the length appropriate in relation to the content? 5 - High/Yes 5 - High/Yes Does the reader get new insights from the article? Please rate the practical significance. Please rate the accuracy of methods. N/A Please rate the statistical evaluation and quality control. 5 - High/Yes Please rate the appropriateness of the figures and tables. Please rate the appropriateness of the references. 5 - High/Yes Please evaluate the writing style and use of language. 5 - High/Yes Please judge the overall scientific quality of the manuscript. 5 - High/Yes Are you willing to review the revision of this manuscript? Yes

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Comments to Authors:

Dear authors.

The manuscript provides a comprehensive overview of workflow detection techniques as well as applications where this techniques can become helpful in near and farther future. It is well written, easily understandable and appropriate references are included. The paper fits very well to Innovative Surgical Sciences with minor revisions:

- in Chapter 2.5, 3.2 and 3.4 the figures are not correctly linked
- images in fig. 3 are not well scaled, resulting in a compressed image
- in tab. 1 you mention informations generated by mechatronic support systems. To my understanding you mix in this table generated "sensor data" by a mechatronic support system (kinematics, video, forces, instruments, operator readiness) with information generated out of this data (measurements [i.e.: here result ist based on video/depthmap or kinematics], actions, tissue structure)
- in chapter 3.4 you mention potential surgical segments for automation, which "should not be too error-sensitive, which means that mistakes or wrong decisions should not have serious consequences". This statement is linked to table 2, where also i.e. anastomotic closure is mentioned. In my opinion, this task is very error sensitive! Please adjust the table.

Reviewer 2: anonymous

Aug 24, 2017

Reviewer Recommendation Term:	Accept with Minor Revision
Overall Reviewer Manuscript Rating:	90
	_
Custom Review Questions	Response
Is the subject area appropriate for you?	5 - High/Yes
Does the title clearly reflect the paper's content?	5 - High/Yes
Does the abstract clearly reflect the paper's content?	4
Do the keywords clearly reflect the paper's content?	4
Does the introduction present the problem clearly?	4
Are the results/conclusions justified?	5 - High/Yes
How comprehensive and up-to-date is the subject matter presented?	5 - High/Yes
How adequate is the data presentation?	4
Are units and terminology used correctly?	N/A
Is the number of cases adequate?	N/A
Are the experimental methods/clinical studies adequate?	N/A
Is the length appropriate in relation to the content?	4
Does the reader get new insights from the article?	5 - High/Yes
Please rate the practical significance.	4
Please rate the accuracy of methods.	N/A
Please rate the statistical evaluation and quality control.	N/A
Please rate the appropriateness of the figures and tables.	5 - High/Yes
Please rate the appropriateness of the references.	5 - High/Yes
Please evaluate the writing style and use of language.	5 - High/Yes
Please judge the overall scientific quality of the manuscript.	5 - High/Yes
Are you willing to review the revision of this manuscript?	Yes

Comments to Authors:

This is a well-written paper which gives a great overview of what surgeons have to expect in the future. Surgical data processing in the meaning as it is presented by the authors will most likely result in increased patient safety. Therefore, the manuscript bears substantial impact for future developments regarding increased intraoperative quality. This may be in particula true for Automatic Understanding of the Surgical Situation (section 3.1)

The paper requires some minor revisions:

- Figure 2 is named two times, please revise in figure 1 and Figure 2 (page 3 of the manuscript)
- For publication the authors should provide enlarged pictures since the ones provided in the manuscript may be too "small" for proper identification
- pages 6, 8 and 9: I do not understand "see Error! Reference source not found." At least to me it remains unclear what the authors mean. It needs clarification.

Authors' Response to Reviewer Comments

Aug 25, 2017

Reviewer #1:

We would like to thank you for your valuable feedback. We will make sure, that no technical blunders (as the wrong figure labels or low-resolution images) will remain in the final version of this paper.

We extended the caption of table 1 to specifically mention measurements and derived data for use in workflow recognition. While depth measurements or tissue structure are clearly secondary data, from our point of view they are all possible inputs to a workflow detection. We avoided terminology like "low and high level" information, as these depend strongly on the specific application, and obviously a workflow phase detected through our method could be analogously an input for another method itself.

We also clarified the mentioned paragraph discussion possible application fields for robotic assistance systems in chapter 3.4. While anastomosis can of course be a source of many complications and adverse effects, the main difficulty lies within the required mechanical precision of the performed movements (which is why we see it as prime option for robotic assistance), while it does not need knowledge-based decisions anymore (such as most situations involving incisions or cuts).

Reviewer #2:

We would also like to thank you for your review and comments. As mentioned above, we will work with the editors to eliminate all technical problems of this article, as the mentioned mistaken figure number and the errors when referencing them.

Reviewers' Comments to Revision

Reviewer 2: anonymous

Aug 26, 2017

Reviewer Recommendation Term:	Accept
Overall Reviewer Manuscript Rating:	90
Custom Review Questions	Response
Is the subject area appropriate for you?	5 - High/Yes
Does the title clearly reflect the paper's content?	5 - High/Yes
Does the abstract clearly reflect the paper's content?	4
Do the keywords clearly reflect the paper's content?	4
Does the introduction present the problem clearly?	4
Are the results/conclusions justified?	5 - High/Yes
How comprehensive and up-to-date is the subject matter presented?	5 - High/Yes
How adequate is the data presentation?	4
Are units and terminology used correctly?	N/A
Is the number of cases adequate?	N/A
Are the experimental methods/clinical studies adequate?	N/A

Is the length appropriate in relation to the content?

Does the reader get new insights from the article?

Please rate the practical significance.

Please rate the accuracy of methods.

Please rate the statistical evaluation and quality control.

Please rate the appropriateness of the figures and tables.

Please rate the appropriateness of the references.

Please evaluate the writing style and use of language.

Please judge the overall scientific quality of the manuscript.

Are you willing to review the revision of this manuscript?

N/A
5 - High/Yes
5 - High/Yes
5 - High/Yes
5 - High/Yes
No: Another revision of the manuscript is not necessary.

4

4

N/A

5 - High/Yes

Comments to Authors:

Thank you for considering the recommendations.