Robot-assisted scaffold implantation and two-stage flap raising of the greater omentum for reconstruction of the facial skeleton: Description of a novel technique

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Abstract

Background: Bone regeneration in the greater omentum is a promising strategy in facial skeleton reconstruction. This feasibility-study aims to perform robot-assisted scaffold implantation and second-stage flap raising.

Methods: Firstly, scaffolds were implanted into the greater omentum using the da Vinci Xi surgical system or conventional technique in five miniature pigs, respectively. After 3 months a free flap including the gastrocolic vascular pedicle was harvested and procedures were evaluated.

Results: The average operation time was 59.2 min for open surgery and 73.8 min for robot-assisted surgery. The average incision length of open surgery was 11.6 cm. Both techniques led to successful scaffold implantation without any complications. In all cases the scaffolds were integrated as intended and resulted in bone formation.

Conclusions: Current study demonstrated that the implantation of scaffolds into the greater omentum and flap harvesting using da Vinci Xi surgical system is a promising minimally-invasive approach in regenerative surgery.

KEYWORDS

free flaps, greater omentum, open surgery, robot-assisted surgery, scaffold-based bone regeneration

1 | INTRODUCTION

The standard of care in facial skeleton reconstruction after ablative oncological treatment or jaw bone osteonecrosis secondary to radiation, antiresorptive medication or severe infection is the use of autologous microvascular bone grafts from the fibula, scapula or iliac crest.1 Autogenous bone harvesting is associated with a risk of donor site morbidity like instability and deformity, muscle weakness and functional limitations.2 Moreover, as the facial skeleton presents a complex three-dimensional anatomy, the shape and extend of bone grafts are insufficient in many cases.3

In recent decades, many approaches to bone cultivation and ectopic endocultivation of bone flaps have been developed as an alternative approach - also to reduce the morbidity of existing therapies.4-6 The reconstruction by endocultivation using 3-dimensional (3D)-printed scaffolds in the greater omentum is a very promising approach in defect-specific bone tissue regeneration.7 This approach is based on tissue engineering strategies aiming...
patient-specific bone reconstruction.\(^8\) In this context, it has not been conclusively clarified in which surgical concept the scaffolds should be implanted into the situs as well as second step flap-harvesting. The greater omentum is a highly vascularised tissue which enables excellent regenerative potential. It has already been established as a free graft for covering large and complicated soft tissue defects in head and neck surgery.\(^9\) Furthermore, the omentum is rich in growth factors and progenitor cells, which enables sufficient proliferation and differentiation reactions whereby scaffolds could be suitable for autologous recellularization and implant in reconstructive surgery.\(^10\) Harvesting the omentum is not associated with any functional deficit; however, open surgery as well as extensive laparotomy results in postoperative morbidity. Robot-assisted surgery is a modern minimally invasive surgical procedure that allows reduction of morbidity through the minimally invasive approach with at the same time excellent optical representation of the surgical field with high-resolution 3D view.\(^11\)

The aim of this study was to evaluate if robot-assisted surgery provides an advantage in the surgical management of scaffolds implantation into the greater omentum and second-step flap raising in facial skeleton reconstruction in regenerative medicine compared to open surgery.

2 | MATERIALS AND METHODS

2.1 | Study design

The study protocol was approved by the Ministry of Energiewende, Landwirtschaft, Umwelt, Natur und Digitalisierung Schleswig-Holstein No. V 242 – 75139/2020 (100-11/20). In total, \(n = 10\) female skeletally mature minipigs were operated: 18 months old, mean bodyweight 41 kg (min. 38 kg, max. 43 kg) (Ellegaard Göttingen Minipigs A/S, Dalmose, Denmark). Five pigs underwent open surgery and five robot-assisted surgery. All operations were performed by one experienced surgical team (Hendrik Naujokat and Robert Bergholz). Outcome parameters were: successful scaffold implantation, procedure time, cutting length and objective recovery time of the pigs. At the second stage procedure the main outcome parameter was successful flap raising including development of a sufficient vascular pedicle.

Recovery of the animals was assessed twice a day by a calibrated team of a veterinarian, an animal keeper and a surgeon based on a preoperative defined score chart which covered four items: bodyweight, general health status, behaviour, evaluation of the surgical site. A score \(<5\) indicates no, \(5–10\) low, \(11–20\) middle and \(>20\) a high burden to animal welfare (Figure 1).

In each animal two scaffolds were implanted into the greater omentum. The scaffolds were of a cylindrical form with a height of 10 mm and a diameter of 12 mm and were additively manufactured out of zirconium-oxide and tricalcium phosphate. Immediately before implantation the scaffolds were loaded in accordance to established protocols\(^7,8\). One scaffold was infiltrated with a collagen gel (RatCol\® Rat Tail Collagen for 3D Hydrogels, Advanced Biomatrix, San Diego, California), the other one with the same collagen gel enriched with 250 \(\mu\)g rhBMP-2 (E. coli derived, Creative Biomart, Shirley, New York) and wrapped by an autogenous periosteum transplant from the forehead (Figure 2).

The general anaesthesia was performed by veterinarians from Christian-Albrechts-University. Intraoperatively, the pigs received 50 mg/kg metamizole i. v. in addition to local anaesthesia as pain medication. Postoperatively, oral pain medication was continued with carprofen (Rimadyl\®) 4 mg/kg for 5 days. The suture material used was Vicryl\® 2-0 (Ethicon Inc., Raritan, New Jersey) and Resolon\® 2-0 (Resorba®, Nürnberg, Germany). Infection control was realized by administration of amoxicillin for 5 days. The sutures were removed 14 days postoperatively during follow-up. The entire study and all operations were performed by an experienced interdisciplinary team, whereby a fair treatment in all cases was ensured.

2.2 | Robot-assisted surgery

In this study a da Vinci XI\® surgical system in the Kurt-Semm-centre for laparoscopic and robot-assisted surgery at the university hospital of Schleswig-Holstein, Campus Kiel was used (Intuitive Surgical Inc., Sunnyvale, CA, USA). The animals were placed supine in foot-deep position and the robot installed on the right-hand side (Figure 3). Three arms were placed along the midline of the upper abdomen using the 8 mm trocars. The 30° videoscope was placed in the middle trocar, the instruments used were Cadiere Forceps (Part number 471049) and a Large SutureCut needle driver (Part number 471296). An additional 15 mm trocar was installed on the left upper abdomen for scaffold insertion (COR 37, Applied medical, Rancho Santa Margarita, CA, USA). The pneumoperitoneum was established with carbon dioxide insufflation with 10 mmHg pressure and a flow of 20 L/min. For scaffold implantation the greater omentum was mobilised and explored for blood vessels. The scaffolds were placed distally to the gastroepiploic vessels (the position influences the length of the vascular pedicle), wrapped by the omentum tissue and secured with resorbable sutures. In the end, the omentum was returned to its natural position and the wound closure was performed in layers (Figure 4).

After 3 months re-entry was performed via the same surgical access for flap raising. Firstly, the intra-abdominal situs was examined regarding adhesions, inflammatory changes, and organ injuries. A free flap was designed including the scaffolds with adjacent omentum tissue, large calibre gastroepiploic vessels and the gastroduodenal vascular pedicle. The greater omentum was detached using a monopolar curved scissors (Part number 470179). The right gastroduodenal vessels were dissected along the outer curvature of the stomach to a sufficient length of at least 8 cm for potential microvascular anastomosis at the recipient site. Side-branches were ligated using the medium clip applier (Part number 470327) and the vascular pedicle was cut. The flap was harvested using an endocatch bag (CD001, Applied medical, Rancho Santa Margarita, CA, USA) that was retracted through the 15 mm trocar-incision. Finally, the animals were euthanised via injection of 60 mg/kg pentobarbital.
2.3 | Open surgery

In conventional surgery the minipigs were placed in supine position and the greater omentum was accessed via a medial laparotomy at the upper abdomen with a safety distance of at least 2 cm to the xyphoid. The procedures for scaffold implantation (mobilising the omentum, placing the scaffolds, fixating the scaffolds) as well as harvesting the free flap were performed analogue to the protocol described above (Figure 5).

2.4 | Statistical analysis

Statistical analyses were performed using SPSS (IBM®, Ehningen, Germany). Normally distributed and non-normally distributed
continuous variables were expressed as mean (±SD), categorical data was presented as total counts. The ratio of surgery time as well as the cutting length and objective recovery time of the pigs were calculated. The relation between variables were evaluated by sample t-test. Associations were considered statistically significant when the p value was <0.05.

3 | RESULTS

All operations, open as well as robot-assisted, could be performed successful without any relevant complications. In both procedures the overview on the surgical field and atraumatic mobilisation of the greater omentum, mainly attached at the greater curvature of the stomach, was easily possible. The insertion of the scaffold, wrapped with the periosteum transplant, could be performed via the additional trocar with the help of an endoscopic grasper. The placement and fixation into the omentum were possible as intended in both accesses. No blood loss worth mentioning was observed in any case.

3.1 | Surgery time and cutting length

The incision-suture-times of the single procedures are presented in Figure 6. The average operation time was 59.2 min for open surgery (±1.3 min) and 73.8 min for robot-assisted surgery (±6.9 min). Statistically, there was no significant difference (p = 0.097). The average incision length of open surgery was 11.6 cm (±0.54 cm, min. 10 cm, max. 13 cm). The incision length of robot-assisted surgery was defined by the count and diameter of the trocars: 3 × 8 mm and 1 × 1 mm.

3.2 | Objective recovery time

The evaluation was performed with the developed score sheet for objective recovery after the first operation. Assessments on the first postsurgical day showed a score of 17 for the open surgery group and 16 for the animals treated by robot-assisted surgery. There was no animal that presented high burden, independent of any treatment.
group. At the second day all animals presented timely recovery with a score of 8 (open surgery) and 5 (robot-assisted surgery) and averages below 5 at the third day. No further intervention than the planned pain medication was necessary.

3.3 | Flap raising

The surgical access for second stage flap raising was performed via the same access that the first stage. Exploration of the abdominal cavity did not reveal any adhesions, inflammatory change or organ lesion after scaffold-implantation. In all cases the scaffolds were located in the greater omentum as implanted, completely integrated and covered by tissue presenting a lot of macroscopically visible vessels and a smooth and remodelled surface. The histological investigation of bone formation inside the scaffolds and biocompatibility of the adjacent tissue were not subject of this study, as the two different methods of implantation had no influence on these parameters. Using the robot-assisted instruments, soft tissue preparation to outline the intended free flap was successful using the monopolar scissors. The development of the vascular pedicle along the greater curvature of the stomach was possible without harming the gastric wall, using the scissors for blunt dissection and clips for ligation of the side branches. However, the clips used in this study were relatively bulky compared to the titanium clips used in open surgery. After preparation of a vascular pedicle of clinically sufficient length the vein was cut first. The venous blood flow did indicate sufficient arterial perfusion and circulation of the flap. The length of the vascular pedicles was between 12 and 16 cm, independent of the surgical procedure, and the diameter of the vessels was from 2.8 to 3.4 mm. Evacuation of the robot-assisted harvested free flap was possible minimally invasive by the endocatch bag without impairing the flap (Figure 7).

4 | DISCUSSION

Minimally invasive surgery has widely demonstrated its benefits in terms of shortened recovery and morbidity regarding abdominal operations. Initial disadvantages as limited manoeuvrability, the presence of rigid instruments and a restricted field of view have been overcome. The da Vinci system was originally used in
abdominal and urological surgery and allows a 3D magnified vision through a binocular stereoscopic endoscope, higher degree of freedom of the instruments and movability of the robot arms in various angles even within confined spaces. Therefore, application of robot-assisted surgery has been extended to various surgical disciplines and indications. To the best of our knowledge, this study is the world-first report on scaffold implantation into the greater omentum for bone tissue engineering and flap raising using robot-assisted surgery.

Nonetheless, robotic surgery is also seen as a challenge and potential risk in the surgical field. It needs a lot of surgical experience and expertise and should not be underestimated. There must always be the possibility to treat the patient in open surgery and to deal with complications. Azadi et al. reported that there are various training curricula, virtual reality simulators and other robotic training tools developed to enhance robotic surgical education and improve surgical skills. Additionally, docking time is a limiting time factor which improves with increasing experience of the surgical team.
our study it was obvious that the duration of the whole surgical procedure using the da Vinci system was similar to that of conventional surgery after the learning curve. Moreover, it is described that robotic surgery can have a shorter learning curve than laparoscopy.\textsuperscript{18} This enables many surgeons to perform laparoscopic approaches to complex procedures, if they would otherwise prefer open surgery and to ensure all patients the best operative treatment.\textsuperscript{19}

In some cases, surgical complications are detected only postoperatively, which increases the mortality and the risk for surgical malpractice.\textsuperscript{20} In this study, no organ injuries, adhesions, or other surgical complications were detected while second-stage procedure for both surgical modalities. Nevertheless, advantages of the robot-assisted surgery as tremor reduction, image magnification, and a stable camera platform lead to less tissue trauma and lower intraoperative blood loss, enable early bowel movements in abdominal surgery, faster mobilisation as well as reduced pain. Minimally invasive approaches have the potential to overcome complications like prolonged wound healing, wound dehiscence and extensive scarring observed in conventional open surgery.\textsuperscript{21–23}

Moreover, a multitude of studies described a shorter recovery time and a reduction of length of hospital stay as advantages of the robotic surgery especially in elderly patients.\textsuperscript{24,25} Usually, patients with oral cancer are elderly patients, undergoing extensive surgery and reconstruction, which is associated with high morbidity and mortality.\textsuperscript{26} After implantation of the scaffolds, the minipigs showed an objectively shorter recovery time, although the animals were active again in both surgical procedures on the second postoperative day. Reduces morbidity is the main reason why the robotic-assisted surgery could be a helpful addition in treatment of patients with an oral tumour needing a bone graft for reconstruction, as conventional procedures are associated with extensive invasiveness, surgical morbidity and a high risk for complications.

It is also obvious that results obtained from animal studies could differ from clinical applications. Therefore, intraoperative complications, postoperative patients’ satisfaction and long-term clinical results should be furtherly assessed.

The greater omentum has been established as a suitable organ in vivo bone regeneration and scaffolds-vascularisation for
reconstruction of the facial skeleton. In the first human cases our group has implanted a titanium mesh filled with hydroxyapatite blocks loaded with bone marrow aspirate and bone morphogenetic protein-2, bone formation has been monitored by SPECT-CT and transplantation to the mandible was performed 3 month later. In this open procedure the upper laparotomy enabled good surgical access to the omentum without impairing adjacent organs, but the patient suffered from some morbidity at the first post surgical days. In these cases, the length of the laparotomy was more than 20 cm. The average length in this animal study was 11.6 cm. Robot-assisted surgery allow minimally invasive access and aesthetic favourable outcomes by small incisions and hiding scars in skin-wrinkles or in the navel. On the other hand, minimally invasive approaches limit the size of the scaffolds possible to implant and to harvest. In our study the scaffolds had a cylindric shape that passed through the 15 mm trocar. Flap harvesting was not possible through the trocar, but through the same incision which had to be dilated only with minimal extend. To engineer a bone flap of a clinically relevant dimension, for example, for a mandibular segmental defect of 7 cm length with a more complex 3D shape, some scaffold-modifications were needed to allow robot-assisted surgery: With the extent mentioned before, it would be desirable to disassemble the entire construct into several segments so that the corresponding scaffolds are implanted one after the other in a certain sort-order through minimally invasive trocars. In the second-step the flap would be prepared as one piece (multiple scaffolds connected by vascularised omentum) and harvested through a small access like a string of beads (e.g. using an endocatch bag) and the entire construct would first be assembled extra-abdominal. This multi-segment approach for bigger bone flaps for reconstruction of the facial skeleton is no longer a problem with today’s CAD/CAM technologies. This animal study is a promising proof of concept that robot-assisted implantation (of more than one scaffold) is a helpful addition to current practice of bone regeneration in the greater omentum due to its minimally invasive approach.

5 CONCLUSION

Despite its limitations, the current study showed that implantation of scaffolds into the greater omentum and second-step flap raising using da Vinci XI system could be a feasible option. Bone tissue regeneration could benefit of robot-assisted surgery regarding surgical outcome, aesthetics, faster mobilisation, shorter hospital stays as well as reducing morbidity. However, further studies are needed to solve the challenge of engineered bone flaps of greater dimensions and the minimally invasive accesses.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

1. Wilkman T, Apajalahti S, Wilkman E, Tornwall J, Lassus P. A comparison of bone resorption over time: an analysis of the free scapular, iliac crest, and tubular microvascular flaps in mandibular reconstruction. J Oral Maxillofac Surg. 2017;75(3):616-621. https://doi.org/10.1016/j.joms.2016.09.009

2. Hennocq Q, Khonsari RH, Vacher C, Nicol P. Twelve-year experience in mandibular reconstruction using osteo-muscular dorsal scapular free flaps. J Plast Reconstr Aesthet Surg. 2021;74(2):259-267. https://doi.org/10.1016/j.bjs.2020.08.124

3. Jie B, Yao B, Li R, An J, Zhang Y, He Y. Post-traumatic maxillofacial reconstruction with vascularized flaps and digital techniques: 10-year experience. Int J Oral Maxillofac Surg. 2020;49(11):1408-1415. https://doi.org/10.1016/j.ijoms.2020.04.012

4. Birkenfeld F, Sengebuch A, Volschow C, Moller B, Naujokat H, Wiltfang J. Scaffold implantation in the omentum majus of rabbits for new bone formation. J Craniofac Surg. 2019;47(8): 1274-1279. https://doi.org/10.1016/j.jcbs.2019.04.002

5. Beck-Broichsitter BE, Becker ST, Seitz H, Wiltfang J, Warnke PH. Endocultivation: histomorphological effects of repetitive rhBMP-2 application into prefabricated hydroxyapatite scaffolds at extra-skeletal sites. J Craniofac Surg. 2015;26(6):981-988. https://doi.org/10.1016/j.jcbs.2015.03.038

6. Warnke PH, Wiltfang J, Springer I, et al. Man as living bioreactor: fate of an exogenously prepared customized tissue-engineered mandible. Biomaterials. 2006;27(17):3163-3167. https://doi.org/10.1016/j.biomaterials.2006.01.050

7. Naujokat H, Loger K, Schulz J, Acil Y, Wiltfang J. Bone tissue engineering in the greater omentum with computer-aided design/computer-aided manufacturing scaffolds is enhanced by a peristome transplant. Regen Med. 2020;15(11):2297-2309. https://doi.org/10.2217/rme-2020-0115

8. Naujokat H, Lipp M, Acil Y, et al. Bone tissue engineering in the greater omentum is enhanced by a peristomial transplant in a miniature pig model. Regen Med. 2019;14(2):127-138. https://doi.org/10.2217/rme-2018-0031

9. Patel RS, Makitch AA, Goldstein DP, et al. Morbidity and functional outcomes following gastro-omental free flap reconstruction of circumferential pharyngeal defects. Head Neck. 2009;31(5):655-663. https://doi.org/10.1002/hed.21016

10. Porzionato A, Sfriso MM, Macchi V, et al. Decellularized omentum as novel biologic scaffold for reconstructive surgery and regenerative
11. Ozkan O, Ozkan O, Cinpolat A, Arici C, Bektas G, Can Ubir M. Robotic harvesting of the omental flap: a case report and mini-review of the use of robots in reconstructive surgery. J Robot Surg. 2019;13(4):539-543. https://doi.org/10.1007/s11701-019-00949-8

12. Giannone F, Felli E, Cherkaoui Z, Mascagni P, Pessaux P. Augmented reality and image-guided robotic liver surgery. Cancers (Basel). 2021;13(24). https://doi.org/10.3390/cancers13246268

13. Park YM, Choi EC, Kim SH, Koh YW. Recent progress of robotic head and neck surgery using a flexible single port robotic system. J Robot Surg. 2021;16(2):353-360. https://doi.org/10.1007/s11701-021-01221-8

14. Bergholz R, Botden S, Verweij J, et al. Evaluation of a new robotic-assisted laparoscopic surgical system for procedures in small cavities. J Robot Surg. 2020;14(1):191-197. https://doi.org/10.1007/s11701-019-00961-y

15. Costello DM, Huntington I, Burke G, et al. A review of simulation training and new 3D computer-generated synthetic organs for robotic surgery education. J Robot Surg. 2021. https://doi.org/10.1007/s11701-021-01302-8

16. Azadi S, Green IC, Arnold A, Truong M, Potts J, Martino MA. Robotic surgery: the impact of simulation and other innovative platforms on operating performance and training. J Minim Invasive Gynecol. 2021;28(3):490-495. https://doi.org/10.1016/j.jmig.2020.12.001

17. Rajanbabu A, Patel V, Anandita A, Burde K, Appukuttan A. An analysis of operating time over the years for robotic-assisted surgery in gynecology and gynecologic oncology. J Robot Surg. 2021;15(2):215-219. https://doi.org/10.1007/s11701-020-01094-3

18. Ind T, Laios A, Hacking M, Nobbenhuis M. A comparison of operative outcomes between standard and robotic laparoscopic surgery for endometrial cancer: a systematic review and meta-analysis. Int J Med Robot. 2017;13(4):e1851. https://doi.org/10.1002/rcs.1851

19. Marcus HJ, Hughes-Hallett A, Payne CJ, et al. Trends in the diffusion of robotic surgery: a retrospective observational study. Int J Med Robot. 2017;13(4):e1870. https://doi.org/10.1002/rcs.1870

20. Wiatrowski R, Kostov S, Alkatout I. Complications in laparoscopic and robotic-assisted surgery: definitions, classifications, incidence and risk factors - an up-to-date review. Wiedeńske Inne Tech Maloinwazyjne. 2021;16(3):501-525. https://doi.org/10.5114/wiitm.2021.108800

21. Sivathondan PC, Jayne DG. The role of robotics in colorectal surgery. Ann R Coll Surg Engl. 2018;100(Suppl 7):42-53. https://doi.org/10.1016/j.ercs.2018.05.002

22. Lefor AK. Robotic and laparoscopic surgery of the pancreas: an historical review. BMC Biomed Eng. 2019;1:2. https://doi.org/10.1186/s42490-019-0001-4

23. Garbarino GM, Costa G, Frezza B, et al. Robotic versus open oncological gastric surgery in the elderly: a propensity score-matched analysis. J Robot Surg. 2021;15(5):741-749. https://doi.org/10.1007/s11701-020-01168-2

24. Palomba G, Dinuzzi VP, Capuano M, et al. Robotic versus laparoscopic colorectal surgery in elderly patients in terms of recovery time: a monocentric experience. J Robot Surg. 2021. https://doi.org/10.1007/s11701-021-01332-2

25. Buchs NC, Addeo P, Bianco FM, Alyoo S, Eili EF, Giulianotti PC. Safety of robotic general surgery in elderly patients. J Robot Surg. 2010;4(2):91-98. https://doi.org/10.1007/s11701-010-0191-1

26. Hertrampf K, Pritzkuileit R, Baumann E, Wilfong J, Wenz HJ, Waldmann A. Oral cancer awareness campaign in Northern Germany: first positive trends in incidence and tumour stages. J Cancer Res Clin Oncol. 2020;146(10):2489-2496. https://doi.org/10.1007/s00432-020-03305-8

27. Wilfong J, Rohnen M, Egberts JH, et al. Man as a living bioreactor: prefabrication of a custom vascularized bone graft in the gastrointestinal omentum. Tissue Eng C Methods. 2016;22(8):740-746. doi.org/10.1089/ten.TEC.2015.0501

28. Kokemuehler H, Spalkhoff S, Noff M, et al. Prefabrication of vascularized bioartificial bone grafts in vivo for segmental mandibular reconstruction: experimental pilot study in sheep and first clinical application. Int J Oral Maxillofac Surg. 2010;39(4):379-387. https://doi.org/10.1016/j.ijoms.2009.08.010