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Research review

A practical guide for small bowel transplantation in rats—review of techniques and models

*Daniel Foell, MD, Felix Becker, MD, Rebecca Hadrian, MD, Daniel Palmes, MD, and Linus Kebschull, MD**

Division of Experimental Surgical Research, Department of General and Visceral Surgery, University Hospital of Muenster, Muenster, Germany

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ABSTRACT

Background: Animal models are a central aspect in research on small bowel transplantation (SBTx). Among them, rats are the preferred species because of their widespread availability and cost effectiveness. Because the complexity of the surgical procedure could per se influence the outcome of an experiment, a standardized and comparable technique is important. Based on of the vast amount of different models and surgical techniques published to this point, a review seemed necessary to guide investigators when choosing the suitable model.

Materials and methods: A systematic literature search of original articles published between 1965 and 2016 using the Medline Database regarding techniques of SBTx in rats was conducted according to the Preferred reporting Items for Systematic Reviews and Meta-Analyses guidelines. Articles describing a new technique or evaluating different techniques were considered.

Results: A total of 38 publications fulfilled the selection criteria and were included. Data from these publications were regarded as too heterogeneous for statistical analysis. Depending on graft length and placement, full-length and reduced length heterotopic and orthotopic models were differentiated. Important factors concerning a good survival rate are the chosen model (heterotopic has a better outcome compared with orthotopic), a vascular flush of the graft *in situ*, a careful luminal flush of the graft, adequate fluid resuscitation, and a warm ischemia time of less than 40 min.

Conclusions: SBTx in rats remains a complex and challenging procedure, which necessitates a standardized technique as well as sufficient training. By choosing the optimal experimental model, applying established strategies, and proven techniques, a standardized and scientifically reliable model can be achieved.

* *Corresponding author*. Division of Experimental Surgical Research, Department of General and Visceral Surgery, University Clinic of Muenster, Albert-Schweitzer-Campus 1, Building W1, Muenster 48149, Germany. Tel.: +49 (251) 83 57248; fax: +49 (251) 8356366.
E-mail address: kebschull@ukmuenster.de (L. Kebschull).

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Introduction

Small bowel transplantation (SBTx) remains the only curative treatment option for patients with terminal intestinal failure.[1] During the last decades, SBTx evolved from an experimental therapy to a routine treatment for highly selected patients in few specialized centers.[2] However, there is an eminent need for further basic research in the sequence of SBTx, which relies on respective animal models to study mechanisms of intestinal failure,[3] the pathophysiology of intestinal ischemia–reperfusion injury,[4] development of new organ conservation strategies,[5] or solely to train and refine surgical techniques. Therefore, various animal models have been developed to study SBTx. Here, rats have proven to be the preferred species because of their cost-effectiveness, availability, and widespread surgical experience with these animals.[6] Since Monchik *et al.* described the first intestinal transplantation in rats in 1971,[7] various technical modifications have been proposed, and diverse heterotopic and orthotopic models have been developed.[8] Along with the complexity and delicacy of the surgical procedure, the diversity of different experimental models complicates the choice for a suitable approach. This review summarizes the literature regarding different rat models of SBTx with a focus on surgical applicability in the experimental setting. We give an up-to-date overview of experimental techniques and models in SBTx, facilitating the researcher's choice of a current approach.

Materials and methods

This review was conducted in adherence to the recommendations published by the "Preferred reporting Items for Systematic Reviews and Meta-Analyses" guidelines.[9] Two independent reviewers conducted selection, data extraction, and critical appraisal of all articles.

Literature search

The present review is based on a systematic analysis of the US National Library of Medicine journal citation database (Medline) via PubMed. PubMed/MEDLINE listed publications from September 1, 1965, to September 1, 2016, describing new surgical techniques or modifications of an existing SBTx model in rats.

The initial Boolean search conducted was as follows:

1. Rats AND small intestine transplantation → 1808 items
2. Rats AND small bowel transplantation → 1860 items
3. Rats AND intestinal transplantation → 2496 items

Therefore, the search was conducted using the following:

1. Rats AND small intestine transplantation AND technique → 148 items
2. Rats AND small bowel transplantation AND technique → 156 items
3. Rats AND intestinal transplantation AND technique → 215 items
4. Rats AND small intestine transplantation AND microsurgery → 78 items
5. Rats AND small bowel transplantation AND microsurgery → 81 items
6. Rats AND intestinal transplantation AND microsurgery → 87 items

Reference lists of relevant studies and other reviews were searched manually; furthermore, the PubMed "related article" function was used.

Study selection

Original articles were positively selected if they mainly described a new surgical technique or evaluated surgical details of the procedure. Neither pure review articles nor articles describing multivisceral transplants were considered. Multiple articles from the same author(s) describing the same or similar approach were only considered once. Only articles in English were included. The full text of all positively selected articles was retrieved, and the reviewers assessed the content in detail.

Data extraction

Two independent reviewers (D.F. and L.K.) performed data extraction from all selected articles, as far as possible. Data of the three following major categories was assessed: (1) animals and model, (2) graft procurement, and (3) recipient procedure.

Results

A total of 38 publications were selected for analysis. Table 1 gives an overview of all selected publications and other relevant data.

Animals and model

Gender

Twenty-eight of 38 authors used male rats.[7,10,15–20,23,25,26,28–32,34,37–46] One group used male donors and female recipients without stating reasons,[24] others did not state the gender of the animal.

Weight

Weight varied broadly from 150 to 400 g, but was most frequently between 200 and 300 g.[12,14,16,17,19,20,25,26,28–30,32,38,40,41,44–46] Some authors used rats with under 200 g bodyweight.[15,24,31,34,35,37] In orthotopic whole bowel SBTx, donors were often smaller than recipients.[10,14,24,30,36,39,41,45–47]

Strain and models

Depending on the study, different inbred or outbred strains were used. In purely *syngeneic models*, (16/38) Lewis (Lew) to Lew[17,24,28,29,32,38,39,45] and Wistar (Wis) to Wis[23,27,34,37,44,46] were most frequently selected.

Allogeneic transplantations (15/38) were performed in varying rejection models. In the original publication by Monchik *et al.*,[7] Lew to Brown Norway (or vice versa) was used. This model was the most frequently transplanted model in this