International Journal of Surgery 22 (2015) 46–53

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Large pore size and controlled mesh elongation are relevant predictors for mesh integration quality and low shrinkage – Systematic analysis of key parameters of meshes in a novel minipig hernia model☆

Dirk Weyhe [a, *], William Cobb [b], Julie Lecuivre [c], Antoine Alves [d], Sebastien Ladet [c], Davide Lomanto [e], Yves Bayon [c]

[a] University Hospital for Visceral Surgery, School VI – Medicine and Health Sciences, Carl von Ossietzky University Oldenburg, Oldenburg, Germany
[b] The Hernia Center, Greenville Health System, Greenville, SC, USA
[c] Covidien – Sofradim Production, 116 Avenue du Formans – BP132, F-01600 Trevoux, France
[d] NAMSA, Chasse sur Rhone, France
[e] Minimally Invasive Surgical Center, National University of Singapore, Singapore

HIGHLIGHTS

- Larger pore size (>1.5 mm) leads to better integration and biomechanical capacity.
- Large pore size and lack of stability in lightweight meshes lead to shrinkage.
- Mesh elongation at 50 N seems to be a new parameter to estimate shrinkage.
- 3D mesh construction leads to high structure stability and low shrinkage.

ARTICLE INFO

Article history:
Received 23 June 2015
Accepted 22 July 2015
Available online 12 August 2015

Keywords:
Biocompatibility
Hernia
Mesh
Pore size

ABSTRACT

Background: Prosthetic mesh implants in hernia repair are frequently used based on the fact that lower recurrence rates are detected. However, an undesirable side effect is persistent foreign body reaction that drives adhesions and shrinkage among other things in the course of time. Thereby a variety of meshes have been created in an attempt to alleviate these side effects, and particular relating to shrinkage, the ideal mesh has not been developed. Large pore size is one of the properties to get better ingrowth of the implants but could also be a risk factor to shrinkage behavior. The aim of this preclinical study was to determine optimal pore size based on mesh integration and shrinkage in a hernia minipig model.
Methods: Twenty female minipigs were each implanted at four abdominal retromuscular sites with meshes (designed and knitted specifically for this study) that had various weights and pore sizes, but similar weave. At 3 and 21 weeks post-operation, ten pigs each were euthanized. Mesh integration and shrinkage were evaluated through macroscopic observation, biomechanical testing and histopathological analysis.
Results: The large pore meshes (6.1–6.6 mm^2) showed significantly better integration than small pore (0.9–1.1 mm^2) counterparts, by biomechanical testing and histological assessment. This was independent of mesh weight. The lightweight small pore mesh exhibited significantly more shrinkage than any of the other meshes, while the three-dimensional heavyweight large pore mesh exhibited the least shrinkage. Mesh shrinkage and elongation at 50 Newton (N) as one parameter of the implant structural stability appeared to be strongly interrelated.
Conclusion: Tissue ingrowth of meshes depends on increasing pore size. Macroporous mesh design >1.5 mm diameter appears to be optimal in terms of mesh integration. Lightweight meshes with a large pore size on one hand and a lack of structural stability on the other hand drives mesh shrinkage. High stretchability (Elongation >50 N) induces higher shrinkage and therefore elongation at 50 N appears to

☆ **Previous Communication**: abstracts & oral presentations at AHS & EHS 2013 meetings.

* Corresponding author. Department for General and Visceral Surgery, Pius Hospital Oldenburg, Georgstr. 12, D 26121 Oldenburg, Germany.
E-mail address: dirk.weyhe@pius-hopspital.de (D. Weyhe).

http://dx.doi.org/10.1016/j.ijsu.2015.07.717

be a new parameter to estimate mesh shrinkage. Three-dimensional mesh constructions relate to the lowest shrinkage behavior caused by higher structure stability.

1. Introduction

Prospective studies demonstrate that reinforcement of tissues with mesh implants is the treatment of choice in hernia repair regarding low recurrence rates, ease of use and morbidity [1]. A rash of those clinical studies allocate the advantages of mesh implantation and therefore international guidelines recommend independent from the surgical technique the use of meshes in groin and ventral hernia repair [2–4]. Despite reducing the incidence of recurrence compared with sutured tissue repair, the use of prosthetic mesh has been associated with chronic groin pain and foreign body sensation and adhesions, as well as shrinkage [5–10]. Up to now, the development of mesh implants was mainly influenced by reduction of material amount to improve their biocompatibility. This lightweight mesh technology based on the assumption that less material leads to less foreign body reaction and fewer undesirable side effects are proven by clinical studies [11]. Nowadays, it is well known that pore size is a key influencing factor of biocompatibility, in terms of mesh integration, scar plate formation, and chronic inflammation [12–14]. A typical phenomenon of scar formation may cause the retraction of the mesh and it is proven in preclinical studies that small pores (<1 mm) induce a connective tissue scar plate which is described as the bridging effect by Klinge and colleagues [15]. Further preclinical studies compared lightweight and heavyweight meshes relating to mesh shrinkage but the relationship of pore size, mesh stability and shrinkage behavior was not considered in those studies [16]. The pore size of commercially available meshes in hernia surgery ranges from 0.4 mm to >3.6 mm, while the majority of the first mesh generation reach a pore size of about 0.8 mm. According to the International EndoHernia Society (IEHS), pore sizes of 1.0–1.5 mm are recommended [4]. To our knowledge the correlation between elasticity, stability porosity of mesh constructions and shrinkage is not proven systematically up to now. This study therefore included a series of two-dimensional (2D) lightweight and heavyweight mesh prototypes and also investigated the comparative value of a large pore three-dimensional (3D) mesh.

Purpose of this experimental study was to define the optimal range of pore size based on the postoperative assessment of tissue integration and shrinkage behavior in a hernia minipigs model.

2. Methods

The study was carried out in strict accordance with the Guide for the Care and Use of Laboratory Animals of the European Institutes of Health (European Directive 2010/63/UE and European Convention of the Council of Europe ETS123). All animal and histology procedures were performed at the Animal Facility of NAMSA (Chasse sur Rhône, France). This protocol was approved by NAMSA Ethical Committee on March 26 and 27, 2012 and the study was carried out at NAMSA (Chasse sur Rhône, France), an accredited facility and registered with the French Department of Agriculture for animal housing, care and investigations.

The authors adhered to ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines.

2.1. Experimental animals

Experiment and analysis were carried out in twenty female Göttingen minipigs (Ellegaard Göttingen Minipigs A/S Dalmose, Denmark). We chose minipigs in this experiment since it is widely acknowledged that these animals make for excellent surgical models because of the high comparability between human and pig anatomy and immunology (see for instance: [17–21]). To avoid false negative results by operating learning curve etc. n = 2/22 minipigs were treated as a pilot scheme. Only animals with initial weight of 34–46 kg (median weight: 39.5 kg), were used. Only healthy animals were selected. Surgeries were performed after 20–22 days of acclimation. The minipigs were housed individually in stainless steel suspended cages (see Section 8), identified by a card indicating the study number, pig number, sex, dates of beginning and end of the study. The animal housing room temperature and relative humidity were recorded daily. The temperature of the room was held between 20 °C and 24 °C. The artificial light cycle was controlled using an automatic timer (12 h light, 12 h dark). There were no significant temperature or relative humidity deviations that adversely affected the health of the animals. Standard veterinary medical care was provided in this study.

2.2. Meshes

To investigate perifilament fibrosis formation (bridging phenomenon) hydrophilic surfaced polymer (polyester) was used. In accordance with the IEHS Guidelines the prototypes consisted of a monofilament structure with different mesh sizes. The five Ø 90-μm monofilament polyester (polyethylene terephthalate; PET) mesh prototypes were designed and knitted specifically for this study. Each differed in pore size and weight while sharing the same weave (Table 1). Lightweight meshes were single monofilament yarn meshes, and heavyweight meshes were double monofilament yarn meshes. The 3D mesh comprised a double layer of single monofilament yarns with single monofilament yarn spacers between each layer. They were all cut in 7×8 cm^2 pieces and sterilized by gamma-irradiation, at a dose of 25–45 kGy. The breaking strength and elongation of the prototypes at 50 N were characterized according to ISO 13934-1:1999 with a Hounsfield H5KS traction machine using the following settings: mesh sample width, 5 cm; initial distance between jaws, 20 cm; velocity of stretching, 100 mm/min; and pre-load, 2 N. Mesh characteristics are reported in Table 1. The test and control articles were provided ready to use.

2.3. Study design

Twenty minipigs were each implanted at four retromuscular implantation sites between the transverse and the internal oblique muscles. Three weeks (10 animals) and 21 weeks (10 animals) post implantation, the minipigs were euthanized. The three-week span was chosen because after this time the mesh typically shows optimal connective tissue development, and the 21-week span was chosen because at this time the mesh is fully remodeled and any scar tissue has completely developed and is healed up. The implanted sites were then macroscopically observed (n = 8 sites per article and per time period) and sampled for histopathological