

THE FATE OF IMPLANTED BIOBRIDGE™ COLLAGEN MATRIX – FINDINGS IN HISTOLOGY, SCANNING, AND TRANSMISSION ELECTRON MICROSCOPY

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ABSTRACT

The technique of lymphangioplasty or capillary thread drainage was historically performed with subcutaneously implanted surgical threads. It has recently been revived by introducing a thread-like aligned nanofibrillar collagen matrix (BioBridge™). These collagen threads constitute subcutaneous neocollectors along which guided lymphangiogenesis is said to occur secondarily. We present for the first time a tissue examination of a 10-month implanted BioBridge™ sample with surrounding tissue from a human subject by histology, scanning and transmission electron microscopy.

Keywords: Minimal invasive surgery, Lymphatic surgery, Lymphangioplasty, BioBridge™, Aligned nanofibrillar collagen

We have previously outlined the history of lymphangioplasty and use of the BioBridge™ collagen matrix for thread lymphangioplasties (in this journal issue). BioBridge™ is in fact the first absorbable material used for this purpose. It is known that in lymphangioplasties performed with non-absorbable threads a fibrous sheath, a sort of capsule, develops around the thread which causes a failure of drainage and recurrence of the lymphedema some time after thread implantation (1-

4). Since no histological or microscopical examination of an implanted BioBridge™ thread in human tissue has yet been reported, we undertook this study based on the availability of the tissue sample and thought the findings might be of some interest.

MATERIALS AND METHODS

The examined tissue specimens were obtained from a patient with secondary (post-oncological) grade 2 lymphedema. The 54 year old patient had undergone a vascularized lymphatic system transfer (transplantation of a free thoracodorsal LYST flap to the thigh) without success. Two years later, liposuction of the thigh and lower leg was performed, along with a lymphangioplasty using 10 BioBridge™ threads. The patient underwent a partial removal of the skin island of the aforementioned LYST flap 10 months later, offering the ability of taking a tissue sample where BioBridge™ had been previously implanted. Samples were obtained from the removed tissue for this analysis with the patient's consent.

RESULTS

Hematoxylin-Eosin Stain

In the hematoxylin-eosin stained samples

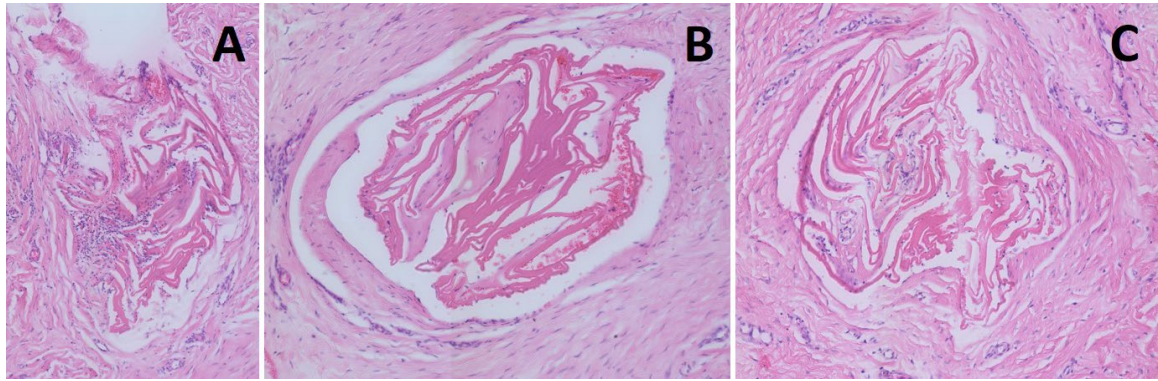


Fig. 1A-C: Hematoxylin-Eosin stained sections displaying BioBridge™ thread and surrounding tissue 10 months after implantation (magnification: 100x).

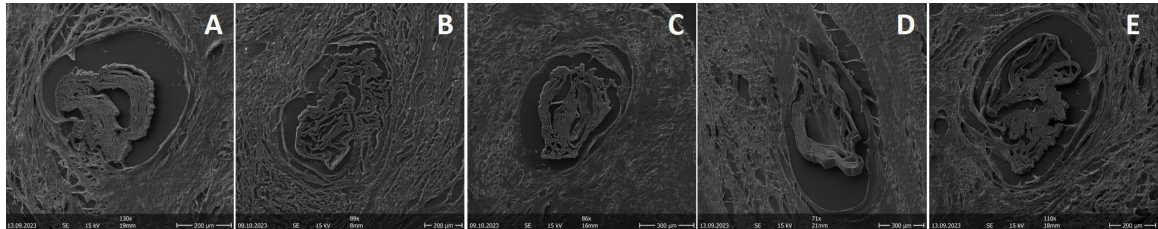


Fig. 2A-E: Scanning electron microscopy from thick paraffin sections (approx. 20-50 μm) displaying BioBridge™ threads and surrounding tissue. After 10 months the threads still appear similar to non-implanted threads (magnifications A-E: 130x, 89x, 86x, 71x, 110x).

(Figs. 1A-C) the characteristically folded tubular structures of the BioBridge™ collagen thread are still identifiable. There is no fibrous sheath around the thread. Visually, there is no evidence of a degradation of the BioBridge™ thread, let alone a complete resorption. There are gaps between the outer layer of the threads and the tissue. Even though these were probably created during the preparation, this suggests that the mechanical cohesion in this area is only moderate.

Scanning Electron Microscopy

For examination by scanning electron microscopy, thicker sections (approx. 20-50 μm) were made from paraffin blocks. A total of 5 regions with BioBridge™ were identified (Figs. 2A-E). The structures found are very well comparable to the non-implanted BioBridge™ specimens (see Figs. 3A-B and previous manuscript in this issue).

The basic structure of BioBridge™ remains largely unchanged (Figs. 3A-D). The surfaces are continuous and even and there are no signs of degradation. The implanted BioBridge™ partly shows a fibrous structure on the surface. It is not possible to clearly determine whether these are fibers of connective tissue formed *in vivo* by the body or whether they are irregularities/changes in the material of the BioBridge™ thread itself.

Transmission Electron Microscopy

For transmission electron microscopy, areas with BioBridge™ were selected and embedded in Epon. In semi-thin cuts, BioBridge™ can clearly be seen (Figs. 4A-B). In detailed enlargement (Fig. 4B), capillary structures (new blood and/or lymph vessels) can be detected within the central tubular cavities of the BioBridge™ thread.

Due to the high magnification and the

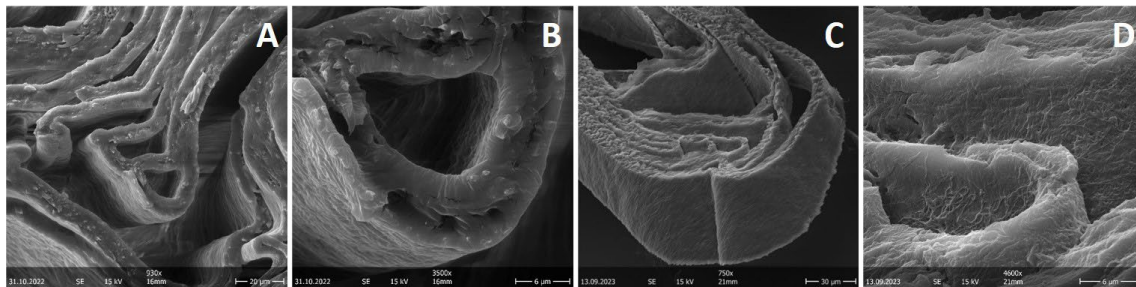


Fig. 3A-D: Scanning electron microscopy of BioBridge™ *in vitro* (3A-B, magnification 930x and 3500x) and of implanted BioBridge™ after 10 months (3C-D, magnification 750x and 4600x). After 10 months, the basic structure of BioBridge™ remains largely unchanged with continuous surfaces and no signs of degradation.

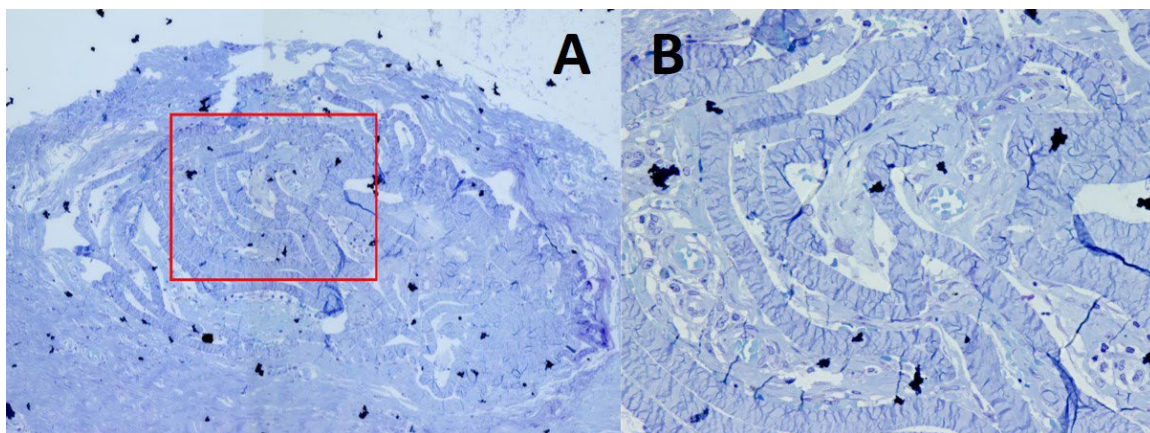


Fig. 4A-B: Light-microscopic image from Epon embedded semi-thin cuts displaying BioBridge™ thread and surrounding tissue 10 months after implantation. Overview (magnification: 100x) in 4A and higher magnification (200x) (4B).

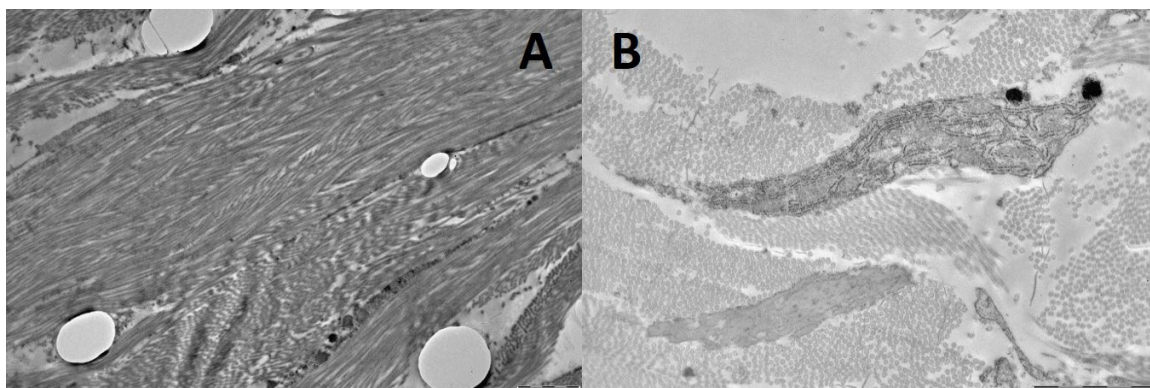


Fig. 5A-B: Transmission electron microscopy displaying BioBridge™ thread and surrounding tissue 10 months after implantation (magnification: 6000x).

associated small field of vision, the structure of BioBridge™ can no longer be captured in total by transmission electron microscopy (Figs. 5A-B). In this degree of magnification (6000x), a fundamental difference between the collagen structures of BioBridge™ and the surrounding tissue could not be determined. This is why a clear demarcation between the BioBridge™ threads and the surrounding tissue is not visible.

Fig. 5A shows densely packed collagen fibers in a layered structure, alternating with longitudinally and transversely oriented fibers, most likely to be assigned to BioBridge™. Collagen fibers were not hit strictly orthogonally here. There are artificial holes in the specimen. Already in the semi-thin cut, BioBridge™ shows some coarser artifacts due to the reembedding. In comparison, Fig 5B shows surrounding connective tissue: orthogonally cut collagen fibers with extensions of fibrocyts and a strand of elastic fibers.

DISCUSSION

In summary, histological examination, scanning and transmission electron microscopy demonstrate that 10 month after implantation, the BioBridge™ thread is still intact without showing any signs of degradation. However, the collagen of the thread is very similar to the surrounding tissue. An integration is partly visible, however, the mechanical cohesion between the thread and the surrounding tissue appears to be fairly weak. There is no fibrous sheath or capsule around the collagen thread. Interestingly, new vessels (blood and/or lymph vessels) can be detected in the central tubular elements of the thread which is a proof of lymph- and hemangeoneogenesis, respectively. This single case should be evaluated with caution for definitive results, but these findings are important for future use and provide a unique view of the potential of lymphangioplasty with BioBridge™ threads.

CONFLICT OF INTEREST AND DISCLOSURE

The authors declare no competing financial interests exist.

REFERENCES

1. Hartley, H, RA Harper: Lymphangioplasty-the fate of silk. *Brit. Med. J.* 27 (1937), 1066-1067.
2. Madden, M, A Ibrahim, AR Ferguson: On the treatment of elephantiasis of the legs by lymphangioplasty. *Brit. Med. J.* 2705 (1912), 1212-1214.
3. Paukshto, MV, C Hadamitzky, T Zaitseva: Development update: A promising surgical procedure for treating secondary lymphedema. *LymphLink* 28 (2015), 12-31.
4. Ziemann SA: *Lymphedema. Causes, Complications and Treatment of the Swollen Extremity.* New York/London 1962, 89-92.

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