Development of biodegradable stents for the treatment of Eustachian tube dysfunction

Abstract: To provide an effective and safe therapy for chronic Eustachian tube dysfunction (ETD), biodegradable stents should be developed to restore important functions, e.g., middle ear ventilation and drainage. After defining general requirements specifications, stent designs of cardiovascular polymeric stents were modified according to dimensions and conditions of the Eustachian tube. Finite element simulations demonstrated the crimping capacity of the developed stent design and the ability of expansion in the specific geometry of the target location. Subsequent in vitro tests of stent prototypes showed satisfying properties concerning crimpability, expansion behavior and elastic recoil to demonstrate general feasibility. Further developments and additional testing will advance the implementation of a new treatment option of ETD.

Keywords: Eustachian tube dysfunction, polymeric stent, finite element analysis, in vitro testing.

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1 Introduction

The Eustachian tube is an approximately 3.5 mm long tube connecting the nasopharynx with the middle ear. It consists of a cartilaginous part nearest to the nasopharynx and a bony part. In the healthy tube the bony part is permanently open; the cartilaginous part is normally closed and opens during swallowing or yawning. Physiologic functions of the Eustachian tube include (i) equalization of atmospheric pressure and ventilation of the middle ear, (ii) protection of the middle ear from pathogens and sounds and (iii) drainage of secretions from the middle ear.

ETD with decreased aeration of the middle ear may lead to acute otitis media (AOM), otitis media with effusion (OME) or chronic otitis media (COM). Reversible functional problems but also structural damage of the middle ear with involved hearing loss can be the consequence. Treatment for ETD includes nasal sprays along with Valsalva maneuver and the placement of tympanostomy tubes in the tympanic membrane. Since 2011, the balloon dilatation of the Eustachian tube as new treatment for ETD has been applied.

Aim of the project presented here is the development of biodegradable Eustachian tube stents to enable an effective therapy of chronic ETD without serious side effects. Therefore, general requirements concerning geometric dimensions and mechanical properties were defined in the first instance. With these specifications stent designs of polymeric cardiovascular stents were modified according to the application in ENT environment. To examine the crimping capacity and expandability of the polymeric stent in the specific geometry of the Eustachian tube, finite element simulations were performed. Subsequent to the fabrication of stent prototypes in vitro testing of the crimping and expansion behavior was conducted.

2 Materials and Methods

2.1 Identification of requirements for Eustachian tube stents

General requirements imposed on Eustachian tube stents regarding geometric dimensions and mechanical properties were ascertained by tomographic analysis and literature
review. Tomographic images for the examination of the Eustachian tube geometry were generated by digital volume tomography (DVT). Measurements of length and cross section of the Eustachian tube were performed and compared to literature data.

2.2 Adaption of stent designs according to Eustachian tube application

Basis for the development of polymeric Eustachian tube stents are cardiovascular stent designs that should be modified according to the defined general requirements for ENT application. One important goal to ensure easy and safe implantation was to minimize the crimp diameter of the stent to increase retention on the balloon catheter and allow passing of application instruments. Therefore, two-dimensional finite element simulations were performed to obtain stent designs in a slightly expanded state with an optimized geometric configuration to allow crimping as well as adequate expansion behavior. Furthermore, the length of the stent was adapted to the application in the Eustachian tube. With the resulting expanded geometry a three-dimensional CAD model of the stent was generated using Creo Parametric 3.0 (PTC, Needham, MA, USA).

2.3 Finite element modeling of the Eustachian tube stent

Using finite element modeling the crimping process with subsequent expansion as well as the implantation of the stent in the Eustachian tube was analyzed to evaluate the performance and mechanical properties of the modified stent design. Therefore, the finite element software LS-DYNA (LSTC, Livermore, CA, USA) was used. For modeling the polymeric stent, the implemented material model SAMP-1 for thermoplastic polymers was applied in conjunction with material data obtained in tensile and compression tests with the PLLA-based stent material [1]. The stent model was meshed in Patran (MSC Software Corporation, Los Angeles, CA, USA) with a global element size of 0.03 mm (figure 1). To determine the crimping capability and minimum attainable diameter of the stent, a finite element simulation of the crimping process was performed. For the reduction of the stent diameter, a displacement boundary condition was applied to a crimping tool, modeled as cylindrical shell with elastic material properties. A nodes-to-surface contact was defined between stent and crimping tool.

Another goal was the evaluation of the expansion behavior of the polymeric stent in the Eustachian tube. Therefore, a simplified CAD model of the Eustachian tube was generated assuming elliptic cross sections with the long and short diameter of tomographic measurements every 2 mm (see figure 2). For finite element analysis, an elastic material model was assigned to the tube. The stent was expanded by applying an increasing pressure on the inside of a balloon catheter, which is modeled as a cylindrical shell with Mooney-Rivlin material model. Between stent and balloon, stent and Eustachian tube as well as Eustachian tube and balloon a one-way surface-to-surface contact was generated.

2.4 In vitro testing of stent prototypes

To evaluate the actual crimping and expansion behavior of the stents, prototypes made of a PLLA-based polymer blend were tested in vitro. The stents were fabricated in a laser cutting process from solution cast mini-tubes (i.d. = 1.4 mm, wall thickness = 150 µm), according to [2].

To minimize stent diameter for implantation and obtain adequate retention of the stent on the balloon catheter, a specific crimping procedure was tested. The stent was positioned on the balloon catheter (nominal dimensions 3.0 x 18 mm) and heated to 50 °C in a temperature chamber. In a first step the hand held crimping tool was set to 1.7 mm. While the balloon was inflated to 2 atm the crimping diameter was steadily reduced to 1.5 mm and held for two minutes. For reduction of elastic recoil of the stent after crimping, which increases the stent diameter, the crimper was set to 1 mm. The
stent was crimped on the balloon again with the same holding time. For the determination of the resulting crimped profile, the prototypes were measured using a non-contact method consisting of a two-axis laser scanner (ODAC 64 XY, Zumbach Electronic AG, Orpund, Switzerland).

In vitro testing of stent expansion was performed using a dedicated test setup according to [3]. In a temperature controlled water bath (37 °C) the balloon was inflated by a computer-controlled pump. Stent profile during balloon inflation and stent recoil at balloon deflation were measured optically with the already mentioned two-axis laser scanner.

Additionally, the stent was expanded using balloon catheters with nominal diameters of 3.5 and 4.0 mm to investigate the maximum stent diameter without strut rupture.

3 Results

3.1 General requirements specification

The Eustachian tube has a total length of approx. 35 mm [4-6], whereby the cartilaginous part, where the stent is supposed to be inserted, constitutes approx. 25 mm. Because the normally closed condition of the Eustachian tube should not be disturbed to preserve valve function and avoid autophony the stent is supposed to end 5-10 mm before pharyngeal orifice, which results in a required stent length of 15-20 mm. Cross-sectional area of the relevant part of ET lumen is in a range of 5-40 mm², which results in an appropriate outer stent diameter of 2.5-7 mm [4, 7]. The elastic recoil of the stent should not exceed about 10 % to ensure adequate wall apposition. To allow passaging of the application instrument, a crimped diameter of the stent system below 1.7 mm should be sought. Investigations regarding the required radial load carrying capacity of the stent in the Eustachian tube will follow in further studies.

3.2 Stent design

Figure 3 shows the initial stent design and the same design in a slightly expanded state generated by two-dimensional finite element simulation and consecutive CAD modeling using the resultant geometry. This design provides increased geometric reserves for crimping that were verified in subsequent three-dimensional in silico analyses.

3.3 Crimping and expansion behavior of stents in silico

Finite element analyses provided the minimal attainable diameter of the stent design. In figure 4 the stent in the crimped state is displayed. The minimum outer stent diameter for the developed stent design is 1.43 mm.

By simulation of the expansion of the stent in the Eustachian tube, induced deformations of the stent should be evaluated. Figure 5 shows the expanded stent in the tube model. As expected, the stent receives an elliptic deformation of the cross-sectional area. Also in the wider part nearest to the nasopharynx, the stent endures this deformation without the risk of strut rupture.
3.4 Performance of stent prototypes in vitro

With the tested crimping procedure at 50 °C the stent could successfully be crimped without damage or collapse. The resultant stent profile was automatically measured (see figure 6) and provided a mean outer diameter of 1.5 mm. The expansion of the stent revealed acute elastic recoil of 7.9 % after balloon deflation. The stent expanded to its nominal diameter of 3.0 mm is displayed in figure 7.

The conducted tests with 3.5 and 4.0 mm balloon catheters showed that the stents in the presented configuration can be safely expanded to a diameter of 3.5 mm without strut ruptures. At 4 mm inner diameter a strut rupture occurred in one end segment of the stent.

Figure 6: Crimped profile of the stent with proximal and distal balloon shoulders

Figure 7: Eustachian tube stent expanded to 3.0 mm

4 Conclusion and Outlook

General requirements for stents to treat ETD were specified. On their basis design modifications of polymeric cardiovascular stent designs were conducted to (i) adapt stent geometry according to Eustachian tube dimension and (ii) enable a sufficiently small crimping diameter to increase retention on balloon catheters and allow passaging of application tools. With the tested specific crimping procedure an outer stent diameter of 1.5 mm could be achieved. The determined elastic recoil after expansion of 7.9 % is below the defined required value of 10 %. The maximum applicable diameter of the stent in the current configuration is 3.5 mm. Depending on the particular tube dimension stents with a bigger target diameter or different stent lengths can be generated in further stage of development.

Future ex vivo cadaver studies will allow the evaluation of the stent performance in the physiological geometry of the Eustachian tube.

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References