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Evaluation of catheter-induced tribological damage to porcine aorta using infra-red spectroscopy

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ABSTRACT

Studies were carried out to assess the potential of attenuated total internal reflection Fourier transform infrared (ATR)-FTIR spectroscopy as a tool for evaluating mechanical-tribological damage to the blood vessel wall occurring during simulated endovascular catheterization on fresh ex-vivo porcine aortic tissue. It is envisaged that this method could be used in laboratory tests to quantitatively compare catheters or catheterization approaches with regard to their effect on damage to the aorta wall.
Tribological damage was induced on the tissue. Obvious changes were visible in the FTIR spectra as well as the friction coefficient as a function of increasing damage. In particular, the spectral changes due to damage to the outermost layer of the tissue were significant, provided appropriate sample conditioning was performed. These changes, which correlated with a reduction in friction coefficient, can be attributed to the removal of successive layers of tissue as a result of a wear process. In conclusion, FTIR spectroscopy was found to be a reliable and effective measurement technique for quantifying catheter-induced tissue damage, allowing very repeatable spectra to be obtained from the tissue up to 36 h after excision with no major spectral changes observed during this time frame due to tissue age.

1. Introduction

Cardiovascular system disease is one of the main health problems and the leading cause of death in European countries. Annually more people die due to cardiovascular failure than from chronic respiratory tract diseases and cancer [1]. Endovascular catheterization is among the key interventions used to treat individuals suffering from cardiovascular diseases such as aortic valve stenosis, coronary heart disease, heart block and abdominal aortic aneurysms [2]. Every year >200 million endovascular catheters are used during endovascular catheterization procedures (ECP) [3]. Complications during ECP can have different origins; however, the most important source of complications, including arterial spasm, cardiac tamponade, hematoma and vascular trauma [4–6], is the mechanical-tribological interaction between the endovascular catheter and the blood vessel wall [7]. Therefore, a deeper understanding of the tissue damage process is needed to study this interaction in detail to look for opportunities to reduce or minimize the aforementioned complications. This in turn will yield faster recovery from surgery, shorter hospital stays, fewer readmissions and lower mortality during ECP.

Several methods have been previously used or may be potentially used to characterize damage to biological tissue arising as a result of the rubbing action of a catheter on its inner surface. These can be broadly classified into two main categories: destructive and non-destructive methods. Destructive tissue damage characterization methods are suitable only for ex-vivo tissue testing and include histology (with chemical or cryogenic tissue fixation) [8], optical (light) microscopy [9], scanning electron microscopy (SEM) [10,11], and environmental SEM [12,13]. Non-destructive methods are more suited for in vivo tissue testing and include techniques such as optical coherence tomography (OCT) [14,15], ultrasound [16], white light interferometry [17], Raman spectroscopy [18,19], and infrared (IR) spectroscopy [20–22]. Of these approaches the most promising for further exploration are the methods based on Raman and IR spectroscopy. However, despite its advantages, Raman spectroscopy has limitations which make it less suitable for tissue damage characterization due to catheterization. In particular, Raman spectroscopy requires the use of microscopy to obtain sufficient signal. This makes it very sensitive to small inhomogeneities that are common in actual tissue. The scattering nature of tissue helps to limit the effect, but in turn reduces the specificity at the surface (where most catheter linked damage is expected to occur). Finally, the largest

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variations expected in tissue are linked to polar bonds, for which Raman spectroscopy is inherently less sensitive than IR spectroscopy.

As a result IR spectroscopy is considered more promising since this technique has a high identification power and can be made surface selective. It has the potential to detect very subtle changes in the biochemical structure of tissue linked to mechanical-tribological damage caused by catheterization, and may be used in vivo.

The main aim of this work is therefore to provide a basis for a spectroscopic method that can be used for in vitro laboratory analysis to compare the damage to the blood vessel wall caused by different catheter designs, materials or catheterization approaches. This should provide the necessary starting point for the optimization of catheter-tissue interaction to limit damage during actual procedures.

2. Background

2.1. Blood vessel wall structure

In order to make sense of spectroscopic differences that are observed as a function of the level of tissue damage encountered it is important to first have a basic understanding of biological tissue, which by its nature is a very complicated, highly variable and inhomogeneous material. To do this it is useful to take a closer look at the actual structure of the blood vessel wall, using aortic tissue as a reference due to its ubiquity in many ECP.

Aortic tissue, in particular, has a strongly stratified structure, which is divided into three layers- the intima, media and adventitia (as encountered by a catheter during arterial perforation from the inside); each of which serves a well-defined purpose:

1. The Intima - is a larger structure composed of three constituents, which together protect the artery wall from the inside and provide reduced friction between the vessel inner lining and blood flowing through the lumen of the artery. Its biochemical composition consists mostly of carbohydrates and proteins. The three constituents of the intima include the following:

   ii. *Glycocalyx* – a negatively charged layer composed of glycoproteins and proteoglycans, performing a wide variety of critical functions in the fluid environment, such as the mechano-transduction of shear stress, exclusion of red blood cells from the endothelial cell (EC) monolayer, modulation of leukocyte attachment and rolling, and inhibition of platelet adhesion. The glycocalyx is roughly 0.5–3.0 μm thick [23]
   iii. *Endothelial cells* – a monolayer of cells, approximately 0.2 μm thick [23].
   iiii. *Internal lamina* – a layer of elastic tissue that separates the intima from the media.

2. The Media - is, volumetrically, the largest layer in the aorta wall. It is a composite layer that is made up of smooth muscle cells and elastic tissue (i.e., layers of crisscrossing elastin strands and collagen fibers embedded in the intercellular matrix). Its main purpose is to allow arterial deformation and recovery (i.e., dilation and contraction) during blood flow. In a biochemical sense the media consists mainly of proteins, carbohydrates, phosphates and to a small extent, lipids.
3. The Adventitia – consists of thick bundles of irregularly distributed collagen fibers in a matrix of fibroblasts, smooth muscle cells, and connective tissue. It provides mechanical resistance to the pulsating blood pressure. Biochemically the adventitia is composed mainly of proteins, phosphates and lipids.

The breakdown of the biological structure, main constituents and biochemical makeup of the arterial wall of the aorta are summarized below in Table 1.

2.2. Definition of mechanical tissue damage levels

When considering mechanical damage to the blood vessel wall occurring during an ECP, it is important to first consider how extensive the tissue damage needs to be in order to be deemed serious. Although this likely varies greatly depending on the state of health of the patient undergoing catheterization, type of blood vessel, age, etc., a benchmark is needed in order to establish a suitable baseline for the observable spectroscopic differences.

A recent study by Sobolewski and El Fray may provide a useful starting point [24]. They point out that the use of a balloon catheter to denude an artery segment has long been utilized as a model of arterial injury and intimal thickening, and explain the mechanisms involved in the healing of the arterial wall after damage. Following arterial injury, platelets and leukocytes are rapidly recruited to the injury site, and within 24 h, smooth muscle cells (SMC) from the media layer begin to replicate, due to a combination of growth factor release from injured SMC, access to blood-born growth factors, and the absence of inhibitory endothelial cell signaling, including nitric oxide. This initial response to injury is then followed by additional SMC migration and proliferation, along with the deposition of extracellular matrix proteins, ultimately leading to the formation of neointima and a stenosis (i.e., narrowing) of the artery.

According to the Sobolewski and El Fray [24], the critical moment in mechanical damaging of the artery wall occurs when the thin intima layer is removed, either by scraping, friction (i.e., abrasion or rubbing), or exposing of the media layer. Based on this finding, in the current study "acceptable" damage is defined as mechanical injury to the arterial wall which does not result in a change in the porcine aortic spectrum from one typical for that of the intima to one typical for that of the media. Any other observable spectrum changes are considered "serious" or "unacceptable" damage, independent of whether they were caused by scraping, abrasion, dissection or perforation of the artery wall.

2.3. Spectroscopic implications of mechanical tissue damage

From a biological point of view it is known what to expect when mechanical damage is inflicted upon the aortic tissue on the basis of knowledge of the main chemical constituents in the tissue which can be summarized as follows [25,26]:

- Proteins that can be found in the media, building collagen and elastin fibers [27].
- Phosphates that, with or without lipids, are building cell plasma membranes or DNA and RNA macromolecules [28].
- Carbohydrates that are present in the tissue in the form of free glycogen (living organism energy source [27]) and in other forms such as the glycocalyx layer in the intima [23].

The spectral signatures for these various tissue constituents are given below, with the regions arbitrarily defined for convenience in the current study [20,22,23,25–33]:

- Region I – Spectral peaks originate mainly from carbohydrates, and to a lesser extent from proteins and phosphates (1130–1000 cm^{-1})
- Region II – Spectral peaks originate mostly from carbohydrates and to a lesser extent from proteins (1180–1130 cm^{-1})
- Region III – Spectral peaks originate mainly from proteins, and to a lesser extent from phosphates and carbohydrates (1360–1180 cm^{-1})
- Region IV – Spectral peaks originate from proteins and carbohydrates (1430–1360 cm^{-1})
- Region V – Spectral peaks originate from proteins (1480–1430 cm^{-1})

When changing between the three main tissue layers, characteristic spectral changes are expected. However, there are large discrepancies in