

AN ANALYSIS OF THE MECHANICAL PARAMETERS OF AN ARTERIOVENOUS FISTULA MODEL

Jonhattan Ferreira Rangel, jferreirarangel01@gmail.com

Kleiber Lima de Bessa, klbessa@ct.ufrn.br

Sandi Itamar Schafer de Souza, sandi@ufrnet.br

Federal University of Rio Grande do Norte. Department of Mechanical Engineering, Center of Technology, Avenida Senador Salgado Filho, 300 – Lagoa Nova, CEP 59078-970 – Natal/RN

Ricardo Wagner da Costa Moreira, ricardowagnermoreira@gmail.com

Federal University of Rio Grande do Norte. Department of Integrated Medicine, Center for Health Sciences, Avenida Nilo Pecanha, s/n – Petrópolis, CEP 59012-300 – Natal/RN

Abstract. *Within the field of research that proposes models for arteriovenous fistula (AVF), more detailed studies are needed due to the wide use of AVF in the treatment of patients with chronic renal failure (CRF). This mechanism can easily become damaged due to the numerous accesses necessary for treatment, and may accrue various problems such as infection, thrombosis, stenosis, hand edema, pseudoaneurysm among others. When the AVF loses its function, a new one must be designed to continue the treatment, which further weakens the patient. The present design uses images generated by computed tomography (CT) scans of a patient with a fistula for the design of a solid model from a rapid prototyping process (3D printing), and then to build a mold for the construction of arteriovenous fistula model, with silicone based material. Mathematical model was applied and It was determined that the model to be manufactured should present the same mechanical properties of an arteriovenous fistula, so that the deformation suffered by an arteriovenous fistula would be the same as that suffered by the silicone model. It was obtained an equivalent thickness of silicon to the actual parameters of a blood vessel. The thickness value was 23,9 μm . Research findings point to a future application in real flow, corroborating the results of associated studies in bioengineering that also aim to promote improvement in the quality of life of patients with chronic renal failure.*

Keywords: *arteriovenous fistula, rapid prototyping process, anastomoses*

1. NOMENCLATURE

AVF	arteriovenous fistula	σ_{θ}	radial stress
d_i	artery diameter	σ_z	longitudinal stress
p_i	pressure internal	r_i	radius internal
h	thickness of the vessel wall	r_e	radius external
ε	deformation	E	Young's Modulus
T	force circumferential	F_R	force longitudinal
F_T	force blood flow		

2. INTRODUCTION

In recent years, there has been an increase in the incidence of patients diagnosed with end stage renal disease, thereby increasing the demand for haemodialysis (Amorim *et al.*, 2013; Frankel, 2006; Noubiap, 2015; Pippias, 2015). Long-term haemodialysis with chronic renal failure is dependent on maintaining patent and functioning vascular access (Sivanesan *et al.*, 1999). Several works in the literature have shown that the arteriovenous fistula (AVF) is the best mechanism for haemodialysis (Krzanowski *et al.*, 2011; Briones *et al.*, 2010; Akoh, 2009). After creating an AVF, blood flow is increased, resulting in a new load request on the AVF wall. The values of wall shear stress and the pressure are elevated causing structural damages in the arteriovenous fistula wall.

In general, hemodynamic forces play a critical role in the physiological responses of endothelial cells. Endothelial cells are subjected to hemodynamic forces, such as shear stress and pressure. To understand the response of endothelial cells to loadings on the cell, several experiments have been and are being carried out in vitro (Chen and Kutys, 2016). Shear stress was studied acting on the endothelial cells through 2D parallel-plate flow chambers and cone-and-plate chamber with monolayers of these cells. These seminal studies revealed that applied shear stress initiated mechanical changes within the cell, such as cellular and cytoskeletal alignment in the direction of the flow (Galbraith *et al.*, 1998). Shear stress acting under endothelial cells regulates its proliferation, gene expression, lipid composition and metabolism, and inflammation (Chien, 2007; Johnson *et al.*, 2011). Changes in blood pressure can create an acute or chronic mechanical stimulus in the form of circumferential stretch. Several studies in the literature have demonstrated that mechanical stretch of different intensities is detected by mechanoreceptors on the cell surface, which enables the conversion of external mechanical stimuli to biochemical signs in the cell. Substantial stretch associated with normal physiological functioning is important in maintaining vascular homeostasis, however, the elevated pressure that occurs

with hypertension exposes cells to excessive mechanical loads, and this may lead to pathological consequences (Jufri *et al.*, 2015;Kaunas *et al.*, 2005) .

Studies have demonstrated that up to 60% of AVFs do not mature (Demer, 2011). The elasticity of the arteries have been investigated and correlated to maturation of the AVF (Sorace *et al.*, 2011; Paulson, 2014; Sorace *et al.*, 2012). In these studies, arterial compliance has been shown to be a strong indicator of vascular disease, cardiovascular disease and renal failure. Arterial stiffening is caused by a change in the ratio of collagen to elastin in the extracellular matrix of the arterial media (Faury, 2001). Sorace *et al.* (2011) and Sorece *et al.*, (2012) showed that the chronic Kidney disease population had significantly lower elasticity (higher elastic modulus, which computes to stiffer vessels) compared to the healthy volunteers with no history of chronic kidney disease. Therefore, this work aims to find the thickness of Sylgard (silicone), which has the same mechanical properties of an arteriovenous fistula.

3. METHODS

For this study, a 3D model of an AVF was constructed as the basis for building a mold, in order to manufacture models of polymeric material, controlling the thickness in order to perform mechanical tests, and to scale out models to own characteristics of real blood vessels.

3.1 Data acquisition

The medical images were obtained by computerized axial tomography scans (CAT scan), provided by the University Hospital Onofre Lopes of Federal University of Rio Grande do Norte (HUOL-UFRN). From the medical images obtained, we developed a three-dimensional composition using the InVesalius software (CTI, Campinas, São Paulo,Brazil).

3.2 Data processing

Computed tomography is an exam that assesses the presence of possible diseases from the analysis of sections obtained by x-ray of the specific body part or limb. Due to the high number of sections, the structural reconstruction with computer processing is extremely expensive, leading researchers to seek solutions that reduce the computer cost without losing necessary details for the next steps of the project (Fig. 1).

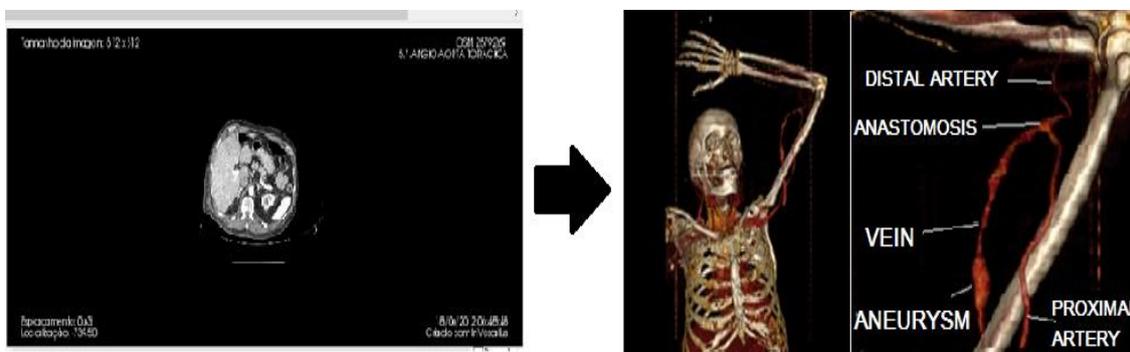


Figure 1. Data acquisition and processing

In efforts to decrease the need for computer processing, the research team decided to decrease the number of sections for the 3D reconstruction of the AVF. This decrease resulted in failures and incongruences in the mesh elements. These failures were corrected using software Autodesk Meshmixer (San Rafael, CA, USA), joining the open elements and improving the surface for 3D printing.

3.3 3D printing

After generating and correcting a three-dimensional computer model, we carried out the manufacturing process of the solid three-dimensional model using the process for rapid prototyping (3D printing) (Fig. 2). The manufacturing was developed in the Laboratory of the *Instituto Metropole Digital* (IMD), ProtoLab (UFRN, Natal - RN, Brazil). This manufacturing process was chosen because of the high degree of complexity of the elements to be manufactured. In addition, it was chose to be able to provide us with the best geometrical and superficial qualities.

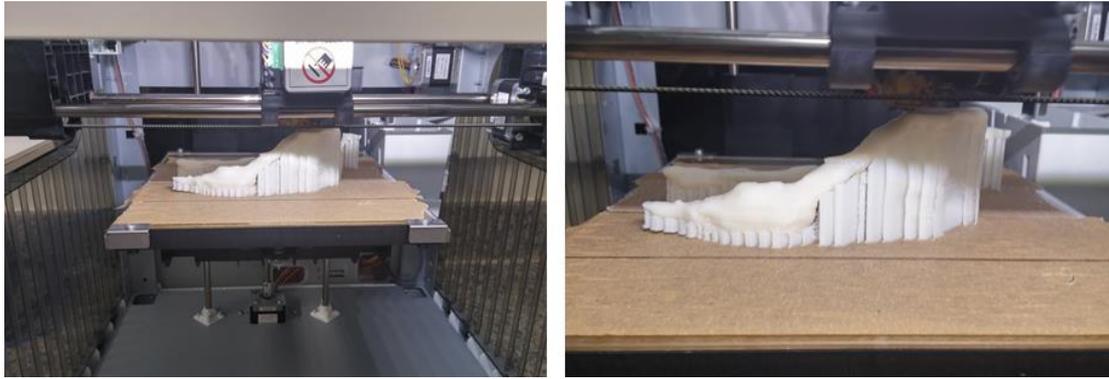


Figure 3. 3D printing.

3.4 Making mold

Once the 3D model was generated, the process of manufacturing the mold was carried out. This served as the basis for making the models to be tested. In this case, we used a two-component elastomer, which, after applying the catalyst, healing occurred at room temperature (Fig. 4).



Figure 4. Elastomer mold

The use of this type of material for making the mold was necessary, despite the higher cost, due to the complexity of the AVF model. This material fits the most complex geometries and provides better demoulding.

3.5 Material of AVF

For the mathematical modeling and manufacturing, the silicone from Dow cornig Sylgard® 184 was chosen. The choice was due to its favorable mechanical characteristics, availability of technical data, in addition to translucency properties, facilitating defect visualization and facilitating the visualization flow in the experiment workbench.

3.6 Biaxial loading: Mathematical Modeling

Due to the flow and pressure conditions present in the blood vessels, longitudinal and circumferential deformations occur on the vessel walls. These deformations are balanced by forces internally developed on the vessel wall, where T is the force used to balance the circumferential deformations and F_r to balance the longitudinal deformations:

$$T = p_i r_i \quad (1)$$

$$F_r = F_T + p_i \pi r_i^2 \quad (2)$$

Analyzing a geometrical model as being a cylindrical tube (Law of Laplace for a cylindrical tube), we have the following equations for strain:

$$\bar{\sigma}_\theta = \frac{p_i r_i}{h} \quad (3)$$

$$\bar{\sigma}_z = \frac{F_T}{\pi h(r_e + r_i)} + \frac{p_i r_i}{2h} \quad (4)$$

where:

$$\sigma = \varepsilon E \quad (5)$$

Assuming that vascular tissue can be considered a homogeneous, isotropic, and linear elastic medium, the intrinsic elastic modulus, E, under small radial strain conditions can be approximated as follows (Weitzel *et al.*, 2009):

$$\varepsilon_{zz} = \frac{\sigma_{zz}}{E} \quad (6)$$

$$\varepsilon_{\theta\theta} = \frac{\sigma_{\theta\theta}}{E} \quad (7)$$

where σ and ε denote tissue stress and strain, respectively. Because stress is difficult to quantify in practice, differences between systolic (P_{sys}) and diastolic (P_{dias}) blood pressure measurements (referred to as pulse pressure, ΔP [mm Hg]) can be used as a surrogate measure (Weitzel *et al.*, 2005). The medium values of the systolic and diastolic blood pressure, internal diameter, elastic modulus, and medium thickness of AVF were obtained from Sorace *et al.* (2012).

It was determined that the model to be manufactured should present the same mechanical properties of an arteriovenous fistula, so that the deformation suffered by an arteriovenous fistula would be the same as that suffered by the model (Sylgard 184). Thus, using the equations above, the desired thickness is achieved.

4 RESULTS

The results presented below were obtained from the consideration of a small deformations, so the term can be neglected F_T (due to flow) in equations 2 and 4. A previously mentioned, in the method, average values of the elastic modulus, and the thickness of the vessel were obtained from SORACE *et al.* (2012): $E_{vessel} = 138.4$ kPa ($n = 75$ patient) and $h_{vessel} = 228$ μ m ($n = 75$ patient). The Sylgard elastic modulus was 1.32 MPa. The pressures and diameters of arteriovenous fistula and the model are the same.

4.1 Arteriovenous fistula 3D

Figure 5 is the arteriovenous fistula obtained from the 3D printer. Clearly, the AVF has extreme and varying diameters. Furthermore, the AVF is not on the same plane. Due to the high degree of processing of the number of DICOM images obtained, we chose to decrease the number of sections obtained by computed tomography. As a result, the surface quality was lost, causing defects in the mesh, which were fixed by software Meshmixer. After the corrections, the AVF was printed. To carry out the experiment, it took approximately 8 hours and 30 minutes, due to the complex geometry of the object under study, beyond the superficial quality (thickening: 0.1mm).

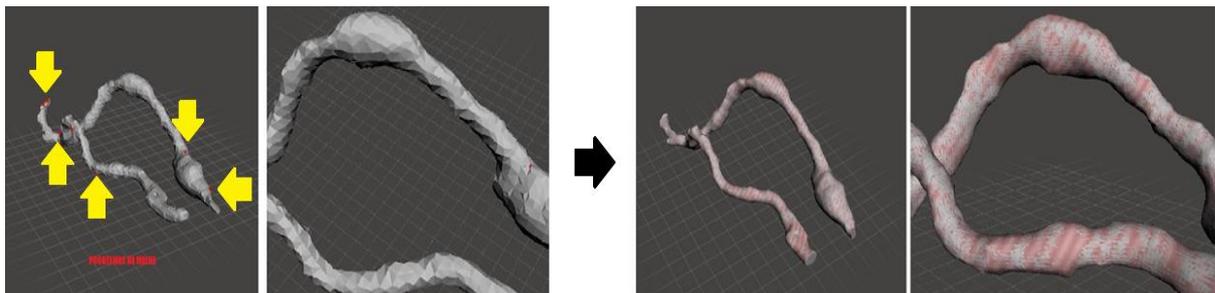


Figure 5. Arteriovenous fistula before and after corrections with Meshmixer.

4.2 Mold elastomer

Figure 6 shows the elastomer mold and arteriovenous fistula paraffin. The procedure was satisfactory, due to the great similarity the arteriovenous fistula obtained from the 3D printer. In the elastomer mold, there are 3 more salient points. These points serve as a guide to the bipartite mold. It sought to perform all of the steps of the process with the best structural and superficial features, in order to obtain models for analysis that approach the maximum of the real blood vessels. After the mold manufacturing has shed paraffin liquid, the models that will serve as the basis for the manufacturing of the blood vessel in silicone with the determined thickness are ready. We chose paraffin, due to its mechanical characteristics, and its low fusion point, facilitating, after curing the silicone, its removal from the inside of the vessel, and the low melting point (50 - 57 ° C), without damaging the mold and allowing for the manufacturing of a large number of models to analyze.



Figure 6. Manufacturing paraffin arteriovenous fistula.

4.3 Mathematical modelling

Mathematical modeling allowed us to determine the thickness of the material (Sylgard 184), taking the same diameter and the same pressure into account. For the calculation of the thickness, equation 7 was used, because it has the greatest deformation. More specifically, the deformation experienced by the vessel in the longitudinal direction is half the radial deformation, whereas the other parameters constant equation. The deformations of the actual vessel and Sylgard 184 vessel, which were matched from that account, obtained the following equations (8):

$$h_{Sylgard} E_{Sylgard} = h_{vessel} E_{Vessel}$$

$$h_{Sylgard} = h_{vessel} \frac{E_{Vessel}}{E_{Sylgard}} \quad (8)$$

$$h_{Sylgard} = 23,9 \mu m$$

Given these equations, it is easy to observe that the modulus of elasticity of Sylgard 184 is around 9.5 times higher than the modulus of elasticity of the vessel. Subsequently, to maintain the equality of equation 8, the thickness of the Sylgard vessel must be less than the thickness of the actual vessel. Therefore, for Sylgard, the thickness value of 23.9 μm was found. This thickness value is about 9.5 times less than the thickness of the AVF.

5 DISCUSSION

The main goal of this study was to build a workbench that simulates the systolic and diastolic pulse, as well as the deformation in an arteriovenous fistula. More specifically, through this work, researchers were able to calculate the thickness of Sylgard 184 to provide the same strain of an arteriovenous fistula. Nonetheless, the continuity of this work was the development of the previously mentioned workbench, and the installation of a strain gage in an arteriovenous fistula using Sylgard 184. The next step of this research is to build another mold for the mathematically calculated thickness of the arteriovenous fistula, and analyze the flow field within the arteriovenous fistula.

To manufacture the silicone arteriovenous fistula with the thickness found will be a challenge. The value found for the thickness is smaller than the thickness of the arteriovenous fistula, this factor is due to silicone elastic modulus is greater than the modulus of elasticity of the arteriovenous fistula.

The motivation to study the flow field within the arteriovenous fistula, as well as deformation and consequently the AVF, indicates the modulus of elasticity, as several studies in the literature present persuasive clinical evidence that these mechanical properties can assist in making the surgeon's decision to fabricate the arteriovenous fistula and ensure their use for a long period of time. Studies show that with decreased elasticity, stiffness of the vessel increases. It is expected that this group has low elasticity correlate with those patients whose arteriovenous fistula will not reach maturity and that there is a greater chance of developing stenosis (Greenwald *et al.*, 1997; Kheda *et al.*, 2009). Park *et al.* (2013) showed that the wall shear rate and circumferential strain were higher for patients with kidney disease compared to healthy subjects.

Therefore, in light of the above, clearly there is a need for a more comprehensive study of the flow field relative to the mechanical properties of the vessel wall to provide data for vascular surgeons on which to base crucial decisions, as well as continuing efforts to improve the quality of life of patients in general.

6. ACKNOWLEDGEMENTS

The authors would like to thank ProtoLab UFRN for making their 3D printer available to us.

7. REFERENCES (Times New Roman, 10pt, bold, upper-case)

- Akoh, J.A., 2009. "Prosthetic arteriovenous grafts for hemodialysis". The journal of vascular access, Vol. 10, No. 3, pp. 137-147.
- Amorim, P., Sousa, G., Vieira, J., Sousa, L., Ribeiro, K., Sobrinho, G., Vieira, T., Meireles, N., Fortes, A., Neves, F., Albino, P., 2013. "Complications of vascular access for hemodialysis - Limits, imagination and commitment". Revista portuguesa de cirurgia cardio-toracica e vascular : orgao oficial da Sociedade Portuguesa de Cirurgia Cardio-Toracica e Vascular, Vol. 20, No. 4, pp. 211-219.
- Briones, L., Diaz Moreno, A., Sierre, S., Lopez, L., Lipsich, J., Adragna, M., 2010. "Permanent vascular access survival in children on long-term chronic hemodialysis". Pediatric nephrology, Vol. 25, No. 9, pp. 1731-1738.
- Chien, S., 2007. "Mechanotransduction and endothelial cells homeostasis: the wisdom of the cell". American Journal of Physiology. Heart and Circulatory Physiology, Vol. 292, No. 3, pp. H1209-H1224.
- Dember, L. M., 2011. "Fistulas First-But Can They Last?". Clinical Journal of the American Society of Nephrology, Vol. 6, No. 3, pp. 463-464.
- Faury, G., 2001. "Function-structure relationship of elastic arteries in evolution: From microfibrils to elastin and elastic fibres". Pathologie-Biologie, Vol. 49, No. 4, pp. 310-325.
- Frankel, A., 2006. "Temporary access and central venous catheters". European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery, Vol. 31, No 4, pp.417-422.
- Fung, Y.C., 1993. Biomechanics: Mechanical Properties of living Tissues. 2^a ed., Springer, San Diego.
- Galbraith, C.G., Skalak, R., Chien, S., 1998. "Shear stress induces spatial reorganization of the endothelial cells cytoskeleton". Cell Motil Cytoskeleton, Vol. 40, pp. 317-330.
- Greenwald, S.E., Moore, J.E. Jr, Rachev, A., Kane, T.P., Meister, J.J., 1997. "Experimental investigation of the distribution of residual strains in the artery wall". Journal of Biomechanical Engineering, Vol. 119, No. 4, pp. 438-444.
- Hibbeler R. C., 2011. Mechanics of Materials, 8^a ed., Prentice Hall, New york.
- Humphrey, J. D., 2001. Cardiovascular Solid Mechanics: Cells, Tissues, and Organs, 1^aed., Springer, Texas.
- Johnson, B.D., Mather, K.J., Wallace, J.P., 2011. "Mechanotransduction of shear in the endothelium: basic studies and clinical implications". Vascular Medicine, Vol. 16, No. 5, pp. 365-377.
- Johnston, I.D., McCluskey, D.K., Tan, C.K.L., Tracey, M.C., 2014. "Mechanical characterization of bulk Sylgard 184 for microfluidics and microengineering". Journal of Micromechanics and Microengineering, Vol. 24, pp 1-6.
- Jufri, N.F., Mohamedali, A., Avolio, A., Baker, M.S., 2015. "Mechanical stretch: physiological and pathological implications for human vascular endothelial cells". Vascular cell, Vol. 7, No. 8 ,pp. 1-12
- Kaunas, R., Nguyen, P., Usami, S., Chien, S., 2005. "Cooperative effects of Rho and mechanical stretch on stress fiber organization". Proceedings of the National Academy of Sciences of the United States of America, Vol. 102, No. 44, pp. 15895-15900.
- Kheda, M.F., Brenner, L.E., Patel, M.J., Wynn, J.J., White, J.J., Prisant, L.M., Jones, S.A., Paulson, W.D., 2009. "Influence of arterial elasticity and vessel dilatation on arteriovenous fistula maturation: a prospective cohort study". Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association – European Renal Association, Vol. 25, No. 2, pp. 525-531.

- Krzanowski, M., Janda, K., Chowaniec, E., Sulowicz, W., 2011. "Hemodialysis vascular access infection and mortality in maintenance hemodialysis patients". *Przegląd lekarski*, Vol. 68, No. 12, pp. 1157-1161.
- Kuts, M.L., Chen, C.S., 2016. "Forces and mechanotransduction in 3D vascular biology". *Current Opinion in Cell Biology*, Vol. 42, pp.73-79.
- Noubiap, J.J., Naidoo, J., Kengne, A.P., 2015. "Diabetic nephropathy in Africa: a systematic review". *World J Diabetes*, Vol. 6, pp. 759-773.
- Oliveira, F.C.M., Bessa, K.L., Moreira, R.W.C., 2015. "Comparison Of Flow Patterns In The Radiocephalic Arteriovenous Fistula Through In Vitro and In Silico Study". *Thermal Engineering*, Vol. 14, No. 2, pp. 07-11.
- Park, D.W., Kruger, G.H., Rubin, J.M., Hamilton, J., Gottschlak, P., Dodde, R.E., Shih, A.J., Weitzel, W.F., 2013. "In vascular wall shear rate and circumferential strain of renal disease patients". *Ultrasound in Medicine and Biology*, Vol. 39, No. 2, pp.241-252.
- Pippias, M., Stel, V.S., Abad Diez, J.M., Afentakis, N., HerreroCalvo, J.A., Arias, M., et al., 2015. "Renal replacement therapy in Europe: a summary of the 2012 ERA-EDTA Registry Annual Report". *Clin Kidney J*, Vol. 8, pp. 248-261.
- Paulson, W.D., 2014. "Does Vascular Elasticity Affect Arteriovenous Fistula Maturation?". *The Open Urology & Nephrology Journal*, Vol. 7, pp. 26-32.
- Sivanesan, S., How, T.V., Black, R.A., Bakran, A., 1999. "Flow patterns in the radiocephalic arteriovenous fistula: an in vitro study". *Journal of Biomechanics*, Vol. 32, No. 9, pp. 915-925.
- Sorace, A.G., Robbin, M.L., Abts, C., Lockhart, M.E., Allon, M., Hoyt, K., 2011. "Arterial elasticity as a predictor for arteriovenous fistula maturation: preliminary results". In *Proceeding of the IEEE International Ultrasonics Symposium Proceedings 2011*, Orlando, FL, USA. Paper no. 6293571.
- Sorace, A.G., Robbin, M.L., Umphrey, H., Abts, C., Berry, J.L., Lockhart, M.E., Allon, M., Hoyt, K., 2012. "Ultrasound Measurement of Brachial Artery Elasticity Before Hemodialysis Access Placement: A Pilot Study". *Journal of Ultrasound in Medicine: Official Journal of the American Institute of Ultrasound in Medicine*, Vol. 31, No. 10, pp. 1581-1588.
- Weitzel, W.F., Kim, K., Rubin, J.M., Xie, H., O'Donnell, M., 2005. "Renal advances in ultrasound elasticity imaging: measuring the compliance of arteries and kidneys in end-stage renal disease". *Blood Purification*, Vol. 23, No. 1, pp. 10-17.
- Weitzel, W.F., Kim, K., Park, D.W., Hamilton, J., O'Donnell, M., Cichonski, T.J., Rubin, J.M., 2009. "High-resolution ultrasound elasticity imaging to evaluate dialysis fistula stenosis". *Seminars in Dialysis*, Vol. 22, No. 1, pp. 84-89.
- Wesly, R.L., Vaishnav, R.N., Fuchs, J.C., Patel, D.J., Greenfield, J.C., 1975. "Static linear and nonlinear elastic properties of normal and arterialized venous tissue in dog and man". *Circulation Research*, Vol. 37, No. 4, pp. 509-520.

8. RESPONSIBILITY NOTICE

The authors are the only responsible for the printed material included in this paper.