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Materials Today: Proceedings 22 (2020) 2696–2703

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ICMMM 2019

Tissue Mimicking Material an Idealized Tissue Model for Clinical Applications: A Review

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Abstract

The Tissue Mimicking Materials (TMM), are widely used in medical research, training, clinical simulators etc., to simulate the properties which are much more similar to that of the real biological tissues. In medical research TMM plays a vital role as the idealized tissue models to design and to test the methods, systems and clinical tools etc. In general TMM are made from bio polymers (agar, agarose, gelatin and gellan gum) and chemically synthesized polymers (polyvinyl alcohol, polymerized siloxanes, poly vinyl chlorides). The bio polymers have the properties of high mass fraction of water (>80%), due to this these biopolymers are not stable for long term use and also have a bacterial growth in a material. On the other hand, the chemically synthesized polymers have a lack of less similar properties to that of the skin. Ratio of softener and polymer, mass fraction of mineral oil and micronized glass beads are factors playing the major role in deciding the properties of TMM. Moreover, by using these TMM the mechanics of needle insertion such as applied force, friction between the needle and tissue and velocity of insertion etc. are studied to use it effectively in clinical applications. Even though, quite number of TMM are developed and tested, the TMM having properties which are very closer to real biological tissue at different aging periods are not available. Therefore, the researchers are working continuously to develop such kind of materials and it needs a depth understanding of available materials and its properties. This paper focuses on presenting a detailed literature study on development and characterization of various TMM, which will be useful for the researchers to develop new TMM for clinical training and clinical tool testing applications.

Peer-review under responsibility of the scientific committee of the 2nd International Conference on Materials Manufacturing and Modelling, ICMMM – 2019.

Keywords: Tissue Mimicking Material; needle insertion; polymers; clinical simulators;

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Nomenclature

TMM	Tissue Mimicking Material
PVA	Poly Vinyl Alcohol
PVC	Poly Vinyl Chloride
PVS	Poly Vinyl Siloxanes
PPG	Poly Propylene Glycol
SEM	Scanning Electron Microscopy
MRI	Magnetic Resonance Imaging
PAMPS	Poly (2-acrylamide-2-methylpropanesulfonic acid)

1. Introduction

Tissue Mimicking Materials are the one of the training phantoms used in clinical applications [1, 2]. TMM are used as one of the general medical practice approaches is subcutaneous insertion of needles and catheters and also they are used as the training phantom's for achieve the experimental results very closer to the actual results with more iterations in the field of needle tip design, needle deflection, deformation of tissues during needle insertion and various applications using needle [3]. In medical field there are more applications of percutaneous needle insertion are biopsies, regional anesthesia, blood sampling, etc. The success of the clinical practice is depend on the accuracy of percutaneous insertion. By using medical simulators such as TMM, it is very helpful to successfully simulate clinical applications with high advantages of medical residents and also used to predetermine the outcome of complicated procedures and find alternative procedure to solve it. By using this kind of simulators the medical residents have more number of opportunities to practice, before perform on a human [4].

To study the needle insertion gellan gum, agar, gelatin, silicon materials, etc. are used as the TMM. Other than these materials due to the optical transparency, appropriate haptic and mechanical properties of PVC, it has been also used as the TMM in the field of needle insertion. Studying the effects of force and deflection of the needle tip during insertion of needle, effect of needle deflection due to insertion speed and the dynamic model is evaluated for bevel tip needle deflection are done by using the PVC as the TMM. The various PVC materials and their compositions are evaluated and designed to improve the PVC materials performance on needle insertion researches [3].

Gellan is the one of TMM, naturally it is a gelling agent and it is also referred as polysaccharide. It is initially founded in the form of linear anionic polymer with have a tetrasaccharide repeating sequence, which consists of two residues of b-D-glucose; are b-D-glucuronate and a-L-rhamnose which are polysaccharide S-60. One of possible variation is molecular weight; its difference widely vary sample to sample in, plant and algal polysaccharides. The varying differences are reflected in growth condition, methods of extraction of the polymer from the tissue matrix, etc. In gellan the molecular weight differences in various sample are genuine [5].

2. Types of TMM

2.1. Agar

Agar is a one of the polysaccharide biopolymer gelling medium; generally it has a more than 80% mass fraction of water. It gives the stability over a temperature range up to 90°C [6, 7]. It is acquired from the algae and generally used in science labs for culinary thickening agent, bacterial growth medium and also used as an impression material in a dental [8, 9]. The nature of the agar is generally two forms. One form is agar powder, is a dry component is added to the mixed solution; are water, glycerol, and benzalkonium chloride. Other form is solid gel; it can be slowly heated till change to liquid [1, 9]. Agar is generally composed from a solution having a 4% of agarose powder in distilled/ deionized water. The phantom is uncontaminated by irradiation to 60 Gy for protect from the growth of bacteria [1, 9, 10]. A higher agar concentration in agar materials are leads to high stiffness and young's modulus. A dissolved agar is presented in phantom, which have an agar component. Mixture of agar and gelatin is used as a constituent for increase in elastography. Phantoms were made with 1%, 2% and 3% dry-weight agar, the

dry-weight concentration of gelatin being 8% in all three homogeneous samples. The samples were congealed by immersing in ice water, and no cross-linking agent was employed to elevate the melting point of the final materials above that of gelatin. The 'compressibility modulus' was monitored for a 4 h period following congealing [11].

2.2. Agarose

Agarose is one of the chemical derivatives of agar which is commonly found in red algae however red algae are limited because of its expensive nature. The disaccharide subunits are formed by glycosidic linkage which is bound by the sugars 3, 6 anhydro-α-L-galactose and β-D-galactose [12, 13]. These disaccharides units repeat to form linear polysaccharides. When physical hydrogels are heated and cooled up to 35°C, agarose are thermally reversible. On increasing the polymer concentration of agarose hydrogels, the modulus of elasticity can be increased. Another factor is that the pore size gets affected because of increase in polymer concentration and thus decreasing the permeability of hydrogels [12, 14].

2.3. Gelatin

Gelatin is derived from natural collagen like porcine skin which is proteinaceous biopolymer gel [6]. Gelatin is the one of the commonly used TMM in commercial phantoms [9]. Melting temperature of the gelatin is around 32°C. The phantom which contains formaldehyde throughout the gelatin, its melting temperature is raised to 78°C. The stability of the dry gelatin is depending on the combination to make it. Gelatin have an osmosis combination is more stable than other similar phantoms. Gelatin is developed from calf skin, deionized water which has an 18 MΩ, CuCl2-2H2O, sodium chloride (NaCl), formaldehyde (HCHO) and antibacterial agent, etc. Table 1 shows the phantasm which has different background materials [11]. By synthesize the gelatin powder and deionized water together, the gelatin gel is achieved. Its formation is simply like that of PVA hydrogel and PVC plastisol. Gelatin powder is to be dissolve in the solution with suitable heating. The special attention is needed to prevent the mixed solution from the air bubbles when transferred into the container. Pour it slowly and ensure there is no bubble formation on the surface and not to trap the bubbles. The formed solution is cooled at 8°C by refrigeration. To bring the properties similar to real biological tissues some additives like sugar free psylliumfiber, cornstarch and sigma cell S5504 cellulose powder are the widely used natural minerals [1, 2, 15-17].

Table 1. Different background materials of Phantasm [11].

Material	Agar	Gelatin	CuCl2-2H2O	EDTA tetra-Nahydrate	NaCl	HCHO	Germall plus	Glass bead scatterers
Phantom B back round	1.17	3.60	0.113	0.33	0.77	0.24	-	4.6
Phantom B back round	1.17	3.60	0.113	0.33	0.77	0.24	1.45	4.6
Phantom C back round	1.17	5.52	0.113	0.33	0.77	0.24	1.45	4.4
Phantom A inclusion	3.53	3.60	0.113	0.33	0.77	0.24	1.45	5.6
Phantom B inclusion	3.53	3.60	0.113	0.33	0.77	0.24	1.45	5.6

2.4. Gellan gum

Gellan gum is also a polysaccharide biopolymer phantom. It has an advantage of highly controllable mechanical properties like toughness, elastic modulus, etc. because of its good efficiency of gelling. Based on the phantom background material composition, three mechanical properties can vary; they are elastic modulus, thermal and electrical conductivity. It has a good thermal conductivity at 120°C [6, 18]. Different thermal conductivity can be attaining by adding polypropylene glycol (PPG) to H_2O. But the condition is PPG is lower thermal conductivity (0.17 W/mK) than water (0.60 W/mK). Thermal conductivity of biological tissue ranges from 0.40 to 0.50 W/mK 0. The elastic modulus can be adjusted to different level because it is well in elastic and also suitable with different kind of modifiers. Table 2 shows the properties of phantoms at different modifiers [6, 20]. By research it has been

proved by adding the oil or PPG to gellan gum, its thermal conductivity becomes reduced. Hence it is act as modifier to change the thermal conductivity in gellen gum related TM phantoms.

Table 2. Properties with different modifier [6, 20].

Denomination	Property	Modifier
Mechanical	Elastic modulus	Gelling agent Salt, sugar
	Fracture toughness	Gelling agent Salt, sugar
Thermal	Melting point	Formaldehyde
	Specific heat	Aluminum powder
Electrical	Conductivity	Metal powder, Carbon and NaCl
	Permeability	Oil, Polyethylene

Nature of the gellen gum is of two forms. One is high-acyl form, it affords soft and texture. In other hand is low-acyl form it deliver the brittle texture and firm phantasm. It is possible to achieve various hardness of phantoms while elastic remains constant by varying the concentration of high-acyl. But it is not exist in low-acyl. It is the best replacement of agar and gelatin phantoms. The various components and its purposes are shown in Table 3 [6].

Table 3. Various components and its purposes [6].

Component	Useful
Gellen gum	Gelling medium, elastic modulus modifier
PPG	Modifier for thermal conductivity
NaCl	Modifier for electrical conductivity

2.5. Polyvinyl Alcohol (PVA)

PVA is the one of non-toxic, hyperbolic and synthetic polymer. In recent engineering the PVA is widely used because it's biocompatibility and repeatability [1, 21]. The tissue phantom was made of silica gel in their work carried out the experiment in two layer phantom, which was composed of PVC lumps and animal meat. Our work also requires the use of tissues mimicking phantom, but the difference is that all of morphology characteristics. Another commonly used tissue mimicking materials are PVA hydrogels. It is a hydrophilic, biodegradable and biocompatible synthetic polymer and it is a most commonly used mimicking material in medical field. In contrast to TMM tissue, a PVA hydrogen phantom is geometrically regular and generally robust used to measure the deflection of needle direct. The degree of polymerization and degree of saponification used in PVA phantom experiment is 2.009 and 97% respectively, and also deionized water is used in preparation of PVA solutions. Mixed solution of dimethyl sulfoxide / deionized water / NACL / were prepared as a solvent. Density of PVA can be measured by using Magnetic Resonance Imaging (MRI) scanning environment. Regular or irregular shaped PVA tissues that were frozen a different number of times could be easily targeted with ultrasound or MR and it can also measure by using the immersion method [21-23].

Morphology evaluation of cortex tissue and PVA hydrogels was performed using Scanning Electron Microscopy (SEM). Each specimen of PVA was sectioned in different view to display the cross sectional image. First the microscope observation of PVA hydrogels with different concentration but same physical crossing linking cycle was performed. Then after first stage, specimen with specific NACL concentration but varying circulations was examined. Samples were sequentially examined placed on the coding stage of SEM [21-24].The formation of resultant PVA hydrogels exhibit a nonlinear viscoelastic behavior and the stress strain characteristics exhibited is similar to that of biological soft tissues [12, 25, 26]. The hydrogels also have mechanical properties including high modulus of elasticity, high tensile strength, and a high tensile modulus. PVA hydrogels achieved a value of tensile strength as 70–100 MPa and a tensile modulus of 2700– 3700 MPa [12, 27]. PVA hydrogels have achieved a modulus value up to 18.4 MPa during the process of compression, and a strain at failure of up to 62% [25]. These

properties are entirely dependent on the water content of the PVA hydrogel, and because of its viscoelastic material, it is also dependent on the strain rate at which the material properties are measured [12].

2.6. Poly Vinyl Chlorides (PVC)

By heating the combination of PVC polymer solution and its softener like diethyl hexyl adipate at certain temperature we can obtain the soft PVC materials. New materials with desired properties can be achieved and designed by modifying the properties of soft PVC materials. By vary the hardness of the soft PVC materials, it is helpful to evaluate the tissues with different mechanical properties and also adjusting the mass ratio of softener and PVC polymer solution, the hardness can be varying. The disadvantage in PVC polymer is it does not have any fluid inside, similar to chemically synthesized polymer which cause the friction during needle insertion. Hence achievement of real biological tissue properties for different age group of people is such challenging one. For achieving the properties similar to real tissues, lubricant agents are added which causes the interstitial fluids in tissue [3, 28]. In researches the mineral oil is used as the lubricant for decrease the friction force during needle insertion with PVC phantoms. To control and prolong monitoring of the needle insertion motion, the ultrasound imaging is a common one. The natural PVC materials are very less similar to tissues because of its speckle formation and by addition of the glass beads into the PVC, the scattering effect is increased and hence it looks realistic in ultrasound imaging but still the overall optical perspicuity of the material is prevented [3].

2.7. Manufacturing of soft PVC

The three major factors of PVC composition can be changed and its effects are studied. They are (1) Ratio between softener and PVC polymer (Rs/p), (2) Mass fraction of mineral oil (Wo) and (3) micronized glass beads (Wg). Soft PVC is generally used in soft parts and it is a non-toxic plastic have a molecular formula $(C_2H_3Cl)_n$ [29]. Mixing of PVC polymer solution and its softener like diethyl hexyl adipate which is opaque solution, heating at a high temperature for vulcanizing and cooling down to room temperature (usually low temperature) the soft PVC is formed. The monomers in the mixed solution are polymerized and it becomes a transparent by heating the solution at high temperature over a range of 100°C [3, 29]. To obtain the various properties of soft PVC, white mineral oil and 50 μm glass beads are added then uniformly mixed. In a research the PVC solution is heated to a temperature range of 150°C by using a heat plate and stirred with help of magnetic stirrer. To avoid rapid change of material properties it can't be overheated; it causes burn the material. After bringing the mixture to the transparent condition, the material can be cooled in a vacuum chamber to avoid the formation of bubble inside. The mixture can be poured into the desired shape and cooled in room temperature. In research the factorial design of experiment is conducted and its results for different levels like low, middle and high is shown in Table 4 [3].

Table 4. Design of experiments at different levels [3].

Factor	Different levels of Experiment		
	Low	Medium	High
Rs/p	0	0.5	1
Wo	0	-	5%
Wg	0	-	1%

The hardness is usually measured by using the durometer (ASTM Standard D2240-05), it is generally used for measure the soft materials like rubber. For measure the soft PVC materials Type 000-S durometer with a sphere surface indenter is used and Soft PVC is assumed as incompressible. The measured hardness is in terms of elastic modulus [3, 6]. The hardness of all tested samples is below 50. The hardness is indirectly proportional to the Rs/p and it does not depend on other two factors. Larger Rs/p samples should have a lower hardness in values. Similarly the other tests like compression and needle insertion are conducted [3].

2.8. Polymerized siloxanes (silicone)

Silicones are the one of the families of synthetic polymers. The polymeric chain called as siloxanes is formed by the addition of silicon links to oxygen (Si-O). The atoms of silicones are generally bonded to methyl, vinyl or phenyl groups; are the one of organic groups [30]. The synthesis of silicone polymer is multifarious. Four steps are involved in formation of silicon polymers (1) Silica reduces to silicon, (2) Chlorosilanes synthesis, (3) Chlorosilanes hydrolysis and (4) Polymerization and polycondensation [10]. The structures of silicones are either linear or cyclic; appealing the thermal stability, chemical inertness and no toxicity [31]. The bonding energy of Si-O is high and it affects the stability. By cross linking of polymer chains, three dimensional networking of silicon can be formed. Cross linking is possible in two different approaches. One manner is condensation crosslink; by persuade moisture in cross linking. Other general one is radical approach, it is feasible only in vinyl groups of silicones [12, 30]. Selection of appropriate cross linkers and filters leads to preferred mechanical properties of silicones are low surface tension [30], 1250 % elongation in its nature length [31], 1.05×10^{-3} GPa tensile modulus [32], 9.8 KN m^{-1} tear strength and range of shear modulus is 210×10^{-6} GPa to 300×10-6 GPa [33].

2.9. Different properties of various TMM

Different types of TMM have different properties; are elastic modulus, tensile strength, failure strain, shear modulus, failure stress, tear strength, flexural modulus, etc. Table 5 shows the tissue phantom materials and its mechanical properties at various testing condition [12].

Table 5. Tissue phantom materials and its mechanical properties [12].

Material used	Mechanical properties						
	Elastic modulus (GPa)		Failure strain		Shear modulus (GPa) $\times10^{-6}$	Tensile strength (MPa)	Tensile stress at failure (MPa)
	Tension	Compression	Tension	Compression			
Agarose	83.7×10^{-6}-3.69×10^{-3}	1×10^{-6}-2.58×10^{-3}	0.11-0.21	0.33-0.44	-	-	-
PVA	2.7-3.7	700×10^{-6}-18.4×10^{-3}	-	45-62%	100-430	70-100	-
Silicones	1.05×10^{-3}	-	325% at failure	-	210-300	-	-
Alginate	-	1×10^{-6}-120×10^{-6}	-	-	2-9	-	3.7×10^{-3}
Chitosan	-	-	10.1-78%	-	-	2.9-6.3	5×10^{-3}-145×10^{-3}
Poly (ethylene glycol) (PEG)	-	500×10^{-6}-0.5	-	-	-	-	-
Poly (2-acrylamide-2-methylpropanesulfonic acid) (PAMPS) and polyacrylamide IPN	-	-	-	92%	-	-	-

Agarose and PVA have an elastic modulus both in tension and compression. It is very helpful to develop the TMM for various kind of age group of people. But Alginate and PEG only have elastic modulus in compression; are 1×10^{-6} GPa for alginate and 500×10^{-6}-0.5 GPa [34] for PEG. The PVA have a high elastic modulus then other type of TMM both in tension (2.7-3.7 GPa) and compression (700×10^{-6}-18.4×10^{-3} GPa). Silicones have a 325% tensile failure strain at failure stage [32]; it is much higher than all. Agarose have very less failure strain; are 0.11-0.21% in tension and 0.33-0.44% in compression. Shear modulus of alginate is 2×10^{-6}-9×10^{-6} GPa; it is very less than other type of TMM. Shear modulus of Silicones ranges from 210×10^{-6} GPa to 300×10^{-6} GPa, it is much higher than PVA.

PVA have more tensile strength, it around 70-100 MPa. PAMPS and polyacrylamide IPN has no elastic modulus, shear modulus, tensile strength and tensile stress at failure [12].

3. Conclusion

This paper reveals the information about the various properties of tissue mimicking materials and its manufacturing methods. It investigated the values of young's modulus, tensile strength, hardness, elastic modulus, needle insertion, friction force, failure stress values of the material, etc. This paper also deals with the mechanical properties of the PVC material, by the influencing of the ratio of softener and polymer solution (Rs/p), the mass fraction of mineral oil used (Wo), and glass beads (Wg). By the observations, to lower the hardness value and elastic modulus of the PVC, the mineral oil could be used and also glass beads have some influences in elastic modulus. Changes in the above value helpful to effectively reduce the friction force, by lubricating the needle insertion procedure. This paper gives the brief outline about various tissue mimicking materials which will be useful for the research community.

References

[1] P. Li, Z. Yang, & S. Jiang, Tissue mimicking materials in image-guided needle-based interventions: A review. Mater. Sci. Eng., C. (2018).
[2] K. Cleary, & T.M. Peters, Image-guided interventions: technology review and clinical applications. Annu. Rev. Biomed. Eng. 12 (2010) 119-142.
[3] W. Li, B. Belmont, & A. Shih, Design and manufacture of polyvinyl chloride (PVC) tissue mimicking material for needle insertion. Procedia Manuf. 1 (2015) 866-878.
[4] N. Abolhassani, R. Patel, & M. Moallem, Needle insertion into soft tissue: A survey. Med. Eng. Phys. 29(4) (2007) 413-431.
[5] E.R. Morris, K. Nishinari, & M. Rinaudo, Gelation of gellan–a review. Food Hydrocolloids. 28(2) (2012) 373-411.
[6] R.K. Chen, & A.J. Shih, Multi-modality gellan gum-based tissue-mimicking phantom with targeted mechanical, electrical, and thermal properties. Phys. Med. Biol. 58(16) (2013) 5511.
[7] A.H. Clark, & S.B. Ross-Murphy, Structural and mechanical properties of biopolymer gels. In Biopolymers (1987) (pp. 57-192). Springer, Berlin, Heidelberg.
[8] R.A. Tomlinson, & Z.A. Taylor, Photoelastic materials and methods for tissue biomechanics applications. Opt. Eng. 54(8) (2015) 081208.
[9] L.M. Cannon, A.J. Fagan, & J.E. Browne, Novel tissue mimicking materials for high frequency breast ultrasound phantoms. Ultrasound Med. Biol. 37(1) (2011) 122-135.
[10] M. De Brabandere, C. Kirisits, R. Peeters, K. Haustermans, & F. Van den Heuvel, Accuracy of seed reconstruction in prostate postplanning studied with a CT-and MRI-compatible phantom. Radiother. Oncol. 79(2) (2006) 190-197.
[11] E.L. Madsen, M.A. Hobson, H. Shi, T. Varghese, & G.R. Frank, Tissue-mimicking agar/gelatin materials for use in heterogeneous elastography phantoms. Phys. Med. Biol. 50(23) (2005) 5597.
[12] K. Bootsma, E. Dimbath, J. Berberich, & J.L. Sparks, Materials Used as Tissue Phantoms in Medical Simulation. (2016).
[13] K.I. Draget, K. Østgaard, & O. Smidsrød, Homogeneous alginate gels: a technical approach. Carbohydr. Polym. 14(2) (1990) 159-178.
[14] K.Y. Lee, & D.J. Mooney, Hydrogels for tissue engineering. Chem. Rev. 101(7) (2001) 1869-1880.
[15] S.L. Chao, K.C. Chen, L.W. Lin, T.L. Wang, & C.F. Chong, Ultrasound phantoms made of gelatin covered with hydrocolloid skin dressing. The J. Emergency Med. 45(2) (2013) 240-243.
[16] J.F. Gerstenmaier, C.J. McCarthy, D. P. Brophy, & C.P. Cantwell, Evaluation of the particulate concentration in a gelatin-based phantom for sonographically guided lesion biopsy. J. Ultrasound Med. 32(8) (2013) 1471-1475.
[17] J.W. Li, M. K. Karmakar, X. Li, W.H. Kwok, & W.D.N. Kee, Gelatin-Agar Lumbosacral Spine Phantom: A Simple Model for Learning the Basic Skills Required to Perform Real-time Sonographically Guided Central Neuraxial Blocks. J. Ultrasound Med. 30(2) (2011) 263-272.
[18] G. Lorenzo, N. Zaritzky, & A. Califano, Rheological analysis of emulsion-filled gels based on high acyl gellan gum. Food Hydrocolloids. 30(2) (2013) 672-680.
[19] F.A. Duck, Physical properties of tissues: a comprehensive reference book. Acad. press. (2013).
[20] N.K. Guimard, N. Gomez, & C.E. Schmidt, Conducting polymers in biomedical engineering. Prog. Polym. Sci. 32(8-9) (2007) 876-921.
[21] H. Miyashita, S. Shimmura, H. Kobayashi, T. Taguchi, N. Asano-Kato, Y. Uchino, ...& K. Tsubota, Collagen-immobilized poly (vinyl alcohol) as an artificial cornea scaffold that supports a stratified corneal epithelium. J. Biomed. Mater. Res Part B: Appl. Biomater: An Off. J. Soc. Biomater, Jpn. Soc. Biomater, and Aust. Soc. Biomater and Korean Soc. Biomater. 76(1) (2006) 56-63.
[22] S.H. Hyon, W.I. Cha, & Y. Ikada, Preparation of transparent poly (vinyl alcohol) hydrogel. Polym. Bull. 22(2) (1989) 119-122.
[23] K.J.M. Surry, H.J.B. Austin, A. Fenster, & T.M. Peters, Poly (vinyl alcohol) cryogel phantoms for use in ultrasound and MR imaging. Phys. Med. Biol. 49(24) (2004) 5529.
[24] S. Jiang, Z. Su, X. Wang, S. Liu, & Y. Yu, Development of a new tissue-equivalent material applied to optimizing surgical accuracy. Mater. Sci. Eng. C. 33(7) (2013) 3768-3774.

[25] J.A. Stammen, S. Williams, D.N. Ku, & R.E. Guldberg, Mechanical properties of a novel PVA hydrogel in shear and unconfined compression. Biomater. 22(8) (2001) 799-806.
[26] W.K. Wan, G. Campbell, Z.F. Zhang, A.J. Hui, & D.R. Boughner, Optimizing the tensile properties of polyvinyl alcohol hydrogel for the construction of a bioprosthetic heart valve stent. Journal of Biomedical Materials Research: An Off. J. Soc. Biomater, The Japn. Soc. Biomater. Aust. Soc. Biomater. Korean Soc. Biomater. 63(6) (2002) 854-861.
[27] N. Teramoto, M. Saitoh, J. Kuroiwa, M. Shibata, & R. Yosomiya, Morphology and mechanical properties of pullulan/poly (vinyl alcohol) blends crosslinked with glyoxal. J. Appl. Poly. Sci. 82(9) (2001) 2273-2280.
[28] N. Hungr, J.A. Long, V. Beix, & J. Troccaz, A realistic deformable prostate phantom for multimodal imaging and needle-insertion procedures. Med. Physics. 39(4) (2012) 2031-2041.
[29] G.M. Spirou, A.A. Oraevsky, I.A. Vitkin, & W.M. Whelan, Optical and acoustic properties at 1064 nm of polyvinyl chloride-plastisol for use as a tissue phantom in biomedical optoacoustics. Phys. Med & Biol. 50(14) (2005) N141.
[30] B.D. Ratner, AS. Hoffman, F.J. Schoen, & J.E. Lemons, Biomater. Science: introduction to Mater. Med. Elsevier. (2004).
[31]A. Rahimi, & A. Mashak, Review on rubbers in medicine: natural, silicone and polyurethane rubbers. Plast. Rubber and Comps. 42(6) (2013) 223-230.
[32] M.DFrogley, D. Ravich, & H.D. Wagner, Mechanical properties of carbon nanoparticle-reinforced elastomers. Compos. Sci. Technol. 63(11) (2003) 1647-1654.
[33] J.C. Lötters, W. Olthuis, P.H. Veltink, & P. Bergveld, The mechanical properties of the rubber elastic polymer polydimethylsiloxane for sensor applications. J. Micromech. Microeng. 7(3) (1997) 145.
[34] W.G. Herrick, T.V. Nguyen, M. Sleiman, S. McRae, T.S. Emrick, & S.R. Peyton, PEG-phosphorylcholine hydrogels as tunable and versatile platforms for mechanobiology. Biomacromolecules. 14(7) (2013) 2294-2304.