Chapter 6

Studies on LSMO nanofluid

Surface functionalized LSMO nanoparticles with improved colloidal stability for hyperthermia applications

N D Thorat¹, V M Khot¹, A B Salunkhe¹, A I Prasad¹, R S Ningthoujam² and S H Pawan¹,²

¹ Center for Interdisciplinary Research, D. Y. Patil University, Kolhapur 416006, India
² Chemistry Division, Bhabha Atomic Research Centre, Mumbai 400085, India

Enhanced colloidal stability of polymer coated La₃ Sr₃.5 MnO₃ nanoparticles in physiological media for hyperthermia application

N.D. Thorat¹, S.V. Otari², R.M. Pardi³, V.M. Khot⁴, A.I. Prasad⁵, R.S. Ningthoujam⁵, S.H. Pawar⁶,⁷

¹ Center for Interdisciplinary Research, D.Y. Patil University, Kolhapur 416006, India
² Chemistry Division, Bhabha Atomic Research Centre, Mumbai 400085, India
6.1. Introduction

Nanofluids are suspensions of nanoparticles in the base fluids, which is a new challenge for applications of nanoparticles in biomedical field provided by nanotechnology. The base fluids are of different types such as water, oil, blood serum and saline. For technical applications oil (ethylene glycol) is widely used and for biomedical applications water, blood serum and saline are commonly used. Nanofluids are fundamentally characterized by the fact that Brownian agitations overcome any settling motion due to gravity. Thus, a stable nanofluid is theoretically possible as long as particles stay small enough (usually <100 nm). Maintaining this size, however, can be a challenge since particles frequently come in to contact with each other potentially leading to the formation of large particle agglomerates which can settle out of suspension. The term “nanofluid” also indicates a mixture where the properties of the nanoparticles and the base fluid contribute to the application [1]. Colloidal suspensions and nanoparticle dispersions these two terms are also used to describe nanofluids. Characterization of nanofluids includes size distributions of nanoparticles in fluid, dispersion stability, concentration and elemental composition of nanoparticles. The most significant application utilizing nano-fluids to date are found in cancer hyperthermia treatment. For cancer hyperthermia research, there are two major areas: nano-vectors and nanofluid hyperthermia (i.e., heat treatment). Both of these require the particles to stay in solution with body fluids until they can target key area.

6.2. Theory of Nanofluid

Practically, a nanofluid can be synthesized by mixing a nanopowder in the base fluid. In reality, the process is more involved. Nanofluids have been synthesized by either a two-step approach that first generates nanoparticles and subsequently disperses them in to base fluids or a one-step physical method that simultaneously makes and disperses the nanoparticles in to base fluids [2].
6.2.1. Synthesis of nanofluids

6.2.1.1. One step method

Direct nanofluid synthesis includes the single batch process which involves the synthesis of nanoparticle, surface modification for stabilization, and transport/mixing with the host liquid. Few methods exist for the preparation of nanofluids through a one step process. These methods include the thermal decomposition of an organometallic precursor in the presence of a stabilizer, chemical reduction, and polyl synthesis. The polyl method is one of the most well-known pathways to noble metal nanoparticles. In the polyl process, a metal precursor is dissolved in a liquid polyl (usually ethylene glycol), after which the experimental conditions are adjusted to achieve the reduction of the metallic precursor by the polyl, followed by atomic metal nucleation and metal particle growth [3-4]. Simple, scalable and environmentally acceptable nanofluid synthesis approaches that consistently meet product specifications are still being developed. Recent progress with “single-step” approaches is promising, but much more work is required to bring nanofluid synthesis to a state where production can be scaled up.

6.2.1.2. Two step method

The preparation of nanofluids begins by direct mixing of the base fluid with the nanomaterials. In the first step, nanomaterials are synthesized and obtained as powders, which are then introduced to the base fluid in a second step. Nanoparticles can be produced from several processes. Some believe that the two step process works well only for nanofluids containing oxide nanoparticles dispersed in de-ionized water as opposed to those containing heavier metallic nanoparticles [3]. Since nanopowders can be obtained commercially in large quantities, some economic advantage exists in using two step synthesis methods that rely on the use of such powders.

6.2.2. Stabilization of nanofluids

The successful applications of nanofluids based on MNPs are dependent on their dispersion stability. Since all prime characteristics of colloidal systems change noticeably in the transition from the dispersed to the aggregated state, the question of stability occupies a fundamental position in colloid science. To achieve the maximum dispersion stability of
nanofluids, it is necessary to stabilize them by using surfactant. The attractive forces between particles can be balanced, and hence particle aggregation prevented, by two mechanisms namely, electrostatic stabilization and steric stabilization. The graphical representation of nanofluidics stabilization techniques are presented in the figure 6.1.

(a) **Steric stabilization**

Steric stabilization can be achieved by surrounding the metal center or surface by layers of material that are sterically bulky, such as polymeric materials. These large adsorbates provide a steric barrier which prevents the metal particles from coming together. Carbon nanotubes and magnetic nanoparticle suspension for nanofluid applications are usually stabilized using the steric mode of stabilization [5].

(b) **Electrostatic stabilization**

The existence of an electric charge on the surfaces of particles is a major source of kinetic stability. The electrostatic stabilization can be achieved by adsorption of ions on to the electrophilic metal surface. The adsorption creates an electrical double/multi-layer which results in a Coulombic repulsion force between the nanoclusters. The electrostatic stabilization is a pH sensitive method and of limited use.

![Diagram](image.png)

**Figure. 6.1.** (a) Representation of steric stabilization of nanoparticles in fluid by surrounding its surface with polymer, (b) Representation of electrostatic stabilization of nanoparticles in fluid.
6.3. Techniques used to study the stability of nanofluid.

Many techniques have been developed to evaluate the stability of nanofluids. The simplest is the sedimentation methods, Zeta potential, Dynamic Light Scattering (DLS), Spectral absorbency analysis (UV-visible spectroscopy) are the other techniques which are used to study the dispersion stability of nanofluids qualitatively.

6.3.1. Sedimentation method

The sediment weight or the sediment volume of nanoparticles in a nanofluid under an external force field is an indication of the stability of the nanofluid. Special instrument is used to study the variation of concentration or particle size of supernatant particle with sediment time. The nanofluids are considered stable when the concentration or particle size of supernatant particles keeps constant. The primary naked eye observation or Sedimentation photograph of nanofluids in test tubes taken by a camera is also a usual method for observing the stability of nanofluids [6].

6.3.2. Zeta potential analysis

Zeta potential measurement allows one to obtain information on the particle surface charge which can be used to study the adsorption of ions on to the particle surface. Zeta potential is electric potential in the interfacial double layer at the location of the slipping plane versus a point in the bulk fluid away from the interface. The potential difference between the dispersion medium and the stationary layer of fluid attached to the dispersed particle is nothing but the zeta potential of the system. The significance of zeta potential is that its value can be related to the stability of colloidal dispersions. So, colloids with high zeta potential (negative or positive) are electrically stabilized while colloids with low zeta potentials tend to coagulate or flocculate. In general, a value of 30 mV (positive or negative) can be taken as the arbitrary value that separates low-charged surfaces from highly-charged surfaces. The colloids with zeta potential from ±30 to 60 mV are believed to be good stable, and those with more than ±60 mV have excellent stability [7-8].
6.3.2.1. Theoretical aspects of zeta potential

The magnitude of the zeta potential gives an indication of the potential stability of the colloidal or well dispersed system. A colloidal system is when one of the three states of matter: solid, liquid and gas are finely dispersed in one of the others. For this technique scientific community is generally interested in the two states of: a liquid dispersed in a liquid, i.e. an emulsion and a solid dispersed in a liquid. If the entire particles in suspension have a large negative or positive zeta potential, then they will tend to repel each other and there is no tendency to flocculate. If the particles have low zeta potential values, then there is no force to prevent the particles confluence and flocculating. The dividing line between stable and unstable suspensions is generally taken at either +30mV or -30 mV.

![Diagram showing zeta potential and stability](image)

**Figure 6.2.** Analysis of colloidal stability of the nanofluid from zeta potential.

As presented in the figure 6.2 the particles with zeta potentials more positive than +30mV or more negative than -30mV are normally considered stable. The primary factor that affects zeta potential is pH. A value of zeta potential without a quoted pH is a virtually meaningless number. Suppose that, the particle in suspension with a negative zeta potential. If further alkali is added to this suspension, then the particles will tend to acquire a more negative charge. If then acid is added to this suspension a point will be reached where the negative charge is neutralized of the characterized system. Any further addition of acid can
cause build up of positive charge in the system. Therefore, a zeta potential versus pH curve will be positive at low pH and negative at high pH.

6.3.2.2. The electrical double layer formation and measurement of zeta potential

The double layer model is used to visualize the ionic environment in the vicinity of a charged colloid and explains the mechanism for formation of electrical repulsive forces. It is easier to understand this model as a sequence of steps that would take place around a single negative colloid if its neutralizing ions were suddenly stripped away. It is necessary to observe the effect of the colloid on the positive ions (counter-ions) in solution. At first, attraction from the negative colloid causes some of the positive ions to form a firmly attached layer around the surface of the colloid; this layer of counter-ions is known as the Stern layer. The typical behaviour of nanofluidics pH dependent zeta potential and isoelectric point is presented in figure 6.3.

![Figure 6.3](image)

**Figure 6.3.** Representation of pH dependent zeta potential and isoelectric point.

Further the positive ions present in the solution are still attracted by the negative colloid, now these positive ions are repelled by the Stern layer as well as by other positive ions that are also trying to approach the colloid. This vibrant equilibrium results in the formation of a diffuse layer of counter ions. The concentration of these ions near the surface is very high, which gradually decreases with distance, until it reaches balance with the counter ion concentration in the colloidal system. In a similar, but opposite, fashion there is a
lack of negative ions in the neighborhood of the surface since they are repelled by the negative colloid. Negative ions are called co-ions since they have the same charge as the colloid [9].

Formation of double layer and its complete overview are presented in figure 6.4. The double layer is created in order to neutralize the charged colloid and, in turn, causes an electro kinetic potential between the surface of the colloid and any point in the mass of the suspending liquid. The voltage difference generated is in the order of mili volts and is referred to as the surface potential. Surface charge and the thickness of the double layer define the magnitude of the surface potential. As we leave the surface, the potential drops off roughly linearly in the Stern layer and in the diffuse layer it is exponentially, approaching zero at the imaginary boundary of the double layer. The potential curve is practically useful because it indicates the strength of the electrical force between particles and the distance at which this force comes into play.

![Figure 6.4](image.png)

**Figure 6.4.** A complete overview of an electrical double layer formation.

This phenomenon is electrophoresis is come into play in colloidal system when charged particle will move with a fixed velocity in an external applied voltage field. The mobility of the particles is related to the electrical potential at the boundary between the moving particle, the liquid dielectric constant and viscosity of the suspending liquid. This
boundary is called the slip plane and is usually defined as the point where the Stern layer and the diffuse layer meet. The Stern layer is considered firmly attached to the colloid, while the diffuse layer is not. Consequently, the electrical potential at this junction is related to the mobility of the particle and is called the zeta potential [10].

6.3.3. Dynamic Light Scattering (DLS) technique

Dynamic Light Scattering (DLS) technique is used to examine the hydrodynamic diameter of nanoparticles suspended in the fluid. The particle sizing mechanism is derived from particle flow characteristics and behaviors, which are a function of the particle size. Particle sizes are divided into two categories with a division around one micron. Submicron particles are governed by Brownian or random motion and particle-particle interactions, but are not generally affected by fluid flow or gravity effects. Interparticle forces or random thermal fluctuations do not influence particles greater than one micron. They are governed by the fluid motion and fluid-particle interactions. For particle sizes much larger than one micron or for particles with densities greater than that of the fluid, gravitational effects become predominant in particle movement [10]. The quantitative and qualitative particle aggregation study is done by DLS in the nanofluids.

6.4. Experimental

The LSMO nanofluid is prepared by two step method. The bare and functionalized LSMO MNPs are prepared and then dispersed in water by ultrasonication. The detailed studies on LSMO nanofluid is done by using zeta potential and dynamic light scattering (DLS) techniques. Zeta potential and dynamic light scattering (DLS) measurements were performed by using a PSS-NICOMP- 380 ZLS (USA) particle sizing system. The particles are diluted to 0.1 wt. % of LSMO. Measurements are taken in water, PBS and NaCl solutions. HCl and NaOH are used to vary the pH from 1 to 12 of the water. The reported zeta potential values are an average of three measurements, each of which is obtained over 30 electrode cycles. The various pH solutions of the PBS (0.01 M) are made accordingly by the protocol.

6.5. Results and discussions
6.5.1. LSMO nanofluid

6.5.1.1. Zeta Potential study

The electrostatic interaction of the nanoparticles can be controlled by variation in their surface charges and it can be determined by measuring the zeta potential of these particles. Figure 6.5 gives the zeta potential of bare LSMO nanoparticles as a function of pH. It showed that the zeta potential of LSMO by PVA is more negative in the range of pH 3–12, while that of LSMO by glycine was positive at lower pH and negative at higher pH.

![Zeta Potential vs. pH](image)

**Figure 6.5.** Zeta potential vs. pH of LSMO nanoparticles synthesized by glycine and PVA in water.

The difference in the zeta potential was due to the chemicals involved in the synthesis process and particle size. The isoelectric point (IEP) was the pH of a dispersion medium of a colloidal suspension at which the colloidal particles carry no net charge or it is normally the point where the colloidal system is least stable. IEP value of LSMO by PVA and LSMO by glycine are approximately 2.5 and 4, respectively. The obtained results show that the LSMO system is more stable in the higher pH and it is believed that addition of base in the suspension creates negative charge on the particles and particles will tend to acquire a more negative charge which increases the repulsive force and results into stable suspension of
LSMO NPs in fluid. The particle agglomeration of LSMO MNPs synthesized by glycine and PVA fuel is presented in the chapter 4 (figure 4.8). The study shows that the LSMO MNPs synthesized by PVA has less agglomeration over the LSMO synthesized by glycine. The average particle diameter for the first one is about 25 nm and 50 nm for later one. So, the zeta potential results imply that the LSMO nanofluid synthesized by PVA fuel is more stable than the LSMO nanofluids synthesized by glycine.

6.5.2. Polymer based LSMO nanofluid

6.5.2.1. Zeta potential study

Figure 6.6 gives the zeta potential of dextran coated LSMO MNPs as a function of pH in water (a) and in PBS (b). From zeta potential study it is observed that the zeta potential values for dextran functionalized LSMO are more negative in the range of pH 3–12. The more negative value suggests that the surface of dextran coated LSMO MNPs consists of OH⁻ group, which comes from dextran [11-12]. At higher pH, the number of OH⁻ increases. The electrostatic repulsion between OH⁻ groups increases and thereby, more negative value in zeta potential arises at higher pH. Isoelectric point (IEP) of dextran functionalized LSMO is approximately at pH 2. The result shows that the dextran functionalized LSMO system is more stable in the higher pH. This is because of hydrogen bonding between oxygen atom of dextran and water molecules with more negative zeta potential value, similar observations are reported in literature [13].

The colloidal stability of the dextran coated LSMO MNPs is evaluated in the biological buffer, i.e. PBS. If the polymer molecule is weakly bonded on the surface of nanoparticles, the phosphate group from the PBS can displace the polymer anchor groups. Thereby, this will reduce steric repulsion and promote flocculation of the nanoparticles due to pair-pair van der Waal’s interactions [14]. Hence, it is necessary to evaluate the colloidal stability of the polymer functionalized MNPs in PBS to study and understanding the efficiency of the grafting of polymer on the surface of MNPs. The observed zeta potential of coated MNPs in PBS at pH 7.4 is -30 mV, which is slightly greater than that in the water at same pH (-28 mV). The well dispersion stability of functionalized LSMO in PBS implies that the anchor groups of the dextran are not have been affected by phosphate salts. The improvement in the zeta potential is because of degree of aggregation of functionalized
LSMO MNPs is higher in the water as compared to biological buffer. The similar observation is reported by Graf et al. and Lim et al. [15-16].

![Graphs showing Zeta potential study](image)

**Figure 6.6.** (a) pH dependent Zeta potential study of dextran functionalized LSMO MNPs in water. (b) Zeta potential of dextran functionalized LSMO MNPs in PBS. (c) Effect of glucose concentration on zeta potential of dextran functionalized LSMO. (d) Functionalized LSMO MNPs NaCl concentration dependent zeta potential values. All values are expressed as mean ± SD, n=3.

The improved Zeta potential obtained in PBS for dextran functionalized LSMO MNPs reveals the strong binding of dextran molecule on the LSMO surface. Zeta potential measurement is an important parameter for implication of nanoparticles as a nanomedicine in the biomedical field. For biological applications, it is required that nanoparticles are stable in the pH 7-8. The dispersion stability study of dextran coated MNPs is evaluated by very few
authors for their use in the biomedical field. Lim et al. coated iron oxide MNPs with dextran and he found the zeta potential after coating is about -23.74 mV to -36.88 mV within the range of pH 4 to pH 13 [16]. In this study, the zeta potential of LSMO coated with dextran is about -29 and -31 mV while for bare LSMO it is about -20 and -23 mV at pH 7 and 8, respectively. These results show that dextran coated LSMO MNPs exhibit the best colloidal stability for biomedical applications among those tested in this work and the results are comparable to the literature.

In human body the normal glucose level is about 8 mg/mL before meal and about 12 mg/mL after meal [17]. Hence, it is necessary to study the effect of glucose concentration on colloidal property of MNPs for their successful In vivo applications. Figure 6.6 (c) represents the zeta potential values of functionalized MNPs in water with addition of different glucose concentrations. The study shows that zeta potential values decreases with increasing glucose concentration. At 7.5 mg/mL and 12.5 mg/mL glucose concentration the values of zeta potentials are about -27 and -25 mV, respectively. Observed value reveals that the colloidal stability of functionalized MNPs is not influenced by the addition of glucose in such concentration range.

The effect of ionic strength on colloidal stability of polymer coated MNPs is one of the primary issues for their successful biomedical applications. The effect of ionic strength (i.e. NaCl concentration) on the stability of dextran coated MNPs is evaluated by using zeta potential technique. The observed values of zeta potential at different NaCl concentrations are shown in the figure 6.6 (d). The starting pH of the solution is 6.7 and it is maintained at 7.4 (physiological pH) to study the effect of NaCl concentration on colloidal stability. The obtained results show that the zeta potential of the solution is gradually transformed from -25 to -15 mV, which implies that the stability of the functionalized MNPs reduces with NaCl concentration from 0.085 to 0.222 M. Therefore, the dextran layer can hinder effectively the aggregation of LSMO MNPs due to the combined steric and electrostatic stabilization, and the resistance against electrolytes is enhanced.

6.5.2.2. DLS study
Figure 6.7 pH dependent hydrodynamic diameter of dextran functionalized LSMO MNPs in water (a) and in PBS (b).

The pH dependent DLS studies of dextran functionalized MNPs in water and in PBS are shown in figure 6.7 (a) and (b), respectively. The results show that hydrodynamic diameters of dextran functionalized LSMO MNPs in water are pH dependent and it ranges from 40-100 nm for pH 12-2. The particle agglomeration study of MNPs in biological buffers, i.e. in PBS is one of the important concerns for In vivo applications. To achieve the possible Invivo applications of functionalized LSMO, efforts are made to study the particle aggregation in PBS and results are shown in figure 6.7 (b). The measured hydrodynamic diameters of the MNPs are about 90, 60, 45 and 40 nm at pH 5.8, 6.6, 7.4 and 8, respectively. The lower hydrodynamic diameter at physiological pH (i.e. at 7.4) reveals the less aggregation which improves the dispersion stability of the functionalized MNPs in PBS. The results obtained from zeta potential and DLS techniques predict the dextran functionalized LSMO MNPs is excellent candidate for the biomedical applications.
6.5.3. Non-Polymer based LSMO nanofluid

6.5.3.1. Zeta potential study

![Graph showing zeta potential vs pH](image)

**Figure 6.8.** pH dependent zeta potential of OA-Betaine HCl functionalized LSMO MNPs in water. All values are expressed as mean ± SD, n=3.

Figure 6.8 gives the zeta potential of functionalized LSMO MNPs as a function of pH. The isoelectric point (IEP) is the pH of a dispersion medium of a colloidal suspension at which the colloidal particles carry no net charge or it is normally the point where the colloidal system is least stable. IEP values of OA-betaine HCl functionalized LSMO are approximately 3.5. The results show that the functionalized LSMO system is well stable in the aqueous medium. Specifically, the N,N,N-trimethyl (\(^+\text{N}-(\text{CH}_3)_3\)) end of betaine coordinates to OA coated LSMO through hydrophobic interaction, while the functionalized exteriors (free \(-\text{COOH}\) groups of betaine) extend into the water medium, granting a high degree of water stability to OA-betaine coated LSMO nanoparticles by forming hydrogen bonds between COOH groups and water. Additionally, the electrostatic repulsive force originating from ionization of the surface functional groups (i.e., \(-\text{COOH}\) groups of betaine) also provide stability to the particles.
Figure 6.9. Effect of NaCl on zeta potential of functionalized LSMO MNPs (a), zeta potential of functionalized LSMO MNPs in PBS at different pH (b), Effect of glucose concentration on zeta potential of functionalized LSMO MNPs (c). All values are expressed as mean ± SD, n=3.

The effect of ionic strength (i.e. NaCl concentration) on zeta potential of OA-betaine HCl functionalized LSMO MNPs is studied. Figure 6.9 (a) represents the zeta potential obtained after addition of NaCl. To study the effect of NaCl concentration on colloidal stability the starting pH of the solution was 6.9 and it maintained at 7.4 (physiological pH). The obtained experimental results show that the zeta potential of the solution is gradually changed from -25 to -13 mV, which implies that the stability of the functionalized MNPs reduces with increase of NaCl concentration from 0.085 to 0.222 M. The dispersion stability of bilayer coated MNPs is also evaluated in the physiological medium (PBS) and obtained results are shown figure 6.9 (b). Zeta potential value of functionalized LSMO MNPs increases with increasing pH of PBS. The Zeta potentials are still high in specified pH of PBS (6.2 – 7.8) and NaCl salt strength. The results show that the functionalization of OA-
betaine HCl on the LSMO MNPs is not much influenced by the salts present in PBS. It is suggested that the strength of coating is strong on the MNPs surface. Figure 6.9 (c) represents the zeta potential values of betaine HCl functionalized MNPs in water with addition of different glucose concentrations. The study shows that zeta potential values decreases with increasing glucose concentration. At 7.5 mg/mL and 12.5 mg/mL glucose concentration the values of zeta potentials are about -19 and -17 mV, respectively. The observed DLS result implies that the colloidal stability of functionalized MNPs is not much influenced by the addition of glucose.

### 6.5.3.2. DLS study

![Graphs showing pH dependent hydrodynamic diameter and effect of NaCl concentration](image)

**Figure 6.10** (a) pH dependent hydrodynamic diameter of OA-betaine HCl functionalized LSMO MNPs in water. (b) Effect of NaCl concentration on hydrodynamic diameter of OA-betaine HCl functionalized LSMO MNPs.

The pH dependent size distribution of functionalized LSMO MNPs in water is measured by DLS technique and obtained results are shown in figure 6.10 (a). From the figure, it is observed the hydrodynamic diameter is 25, 90, 60, 40 and 30 nm at pH 2, 4, 6, 8 and 10, respectively. The observed hydrodynamic diameter at pH 7-10 is less for functionalized LSMO MNPs, which implies that the aggregation of the functionalized LSMO is less and it results in to the improvement in colloidal stability of the LSMO MNPs. The
same propensity is observed in the zeta potential study, so the zeta potential and DLS measurements predict that the dispersion stability of the OA-betaine HCl functionalized LSMO MNPs is improved in the aqueous medium. The NaCl concentration (ionic strength) dependent DLS results are shown in the figure 6.10 (b). It is observed from the results that, with increasing NaCl concentration, particle aggregation increase. This is because NaCl molecules reduce the thickness of coating as a result aggregation is increased due to loss of steric repulsion.

6.6. Summary

The present chapter describes the colloidal stability study of LSMO nanofluids. The Zeta potential and DLS techniques are employed to study the colloidal stability. LSMO MNPs synthesized by glycine fuel is least stable compared to LSMO MNPs synthesized by PVA fuel. To improve the colloidal stability of LSMO MNPs synthesized by PVA, polymeric and non-polymeric functionalization is done on the surface of MNPs. It is observed that the both types of functionalization improves the colloidal stability of bare LSMO nanofluid. In detail study on effect of ionic strength and different physiological conditions are evaluated. The colloidal stability study of functionalized LSMO nanofluid in the presence of NaCl and PBS shows that the stability of is not greatly influenced by the ionic strength. So, the chapter concludes that, the strategy of polymeric and non polymeric functionalization on bare LSMO MNPs is a great potential as a nanofluid for hyperthermia application.
References


