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Donor heart vitrification with magnetic nanoparticles, ice binding proteins and alternating magnetic energy: A preliminary step towards a donor heart bank

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After 50 years after the first human heart transplantation there has been significant progress in the field over the last years. The 1-yr survival rates following heart transplantation have improved from 30% in the 1970s to almost 90% in the 2000s, and heart transplantation continues to be the gold standard treatment for heart failure disease, but the waiting lists represent only a small fraction of the patients who would benefit from the procedure. there are still many challenges that we are currently facing in heart transplantation. regarding organ shortage, donor heart acceptance criteria have been reconsidered, and better donor management could increase the organ pool, maximizing the use of hearts recovered from cadaveric donors, but demand for heart transplantation is strong and growing, and transplant programs cannot meet patient demand, leaving many to die on the waiting list. for every 10 patients transplanted with a new heart, nearly 4 died waiting and another 19 are still waiting and only 3 out of 10 organ donors hearts are transplanted. actually, this is one of the main challenges in heart transplantation in the world, and cryopreservation/ vitrification could well be one of the potential future solutions. additionally, one of the main challenges in cryobiology is the cryopreservation of complex tissues and bulky organs. on the other hand, cells in suspension are simpler to cryopreserve and recently campbell et al. cryopreserved whole sheep ovaries with restoration of ovarian function and fertility. despite all these achievements, the long-term preservation of organs has not been attained yet in a routine way. the advances in the last two decades point to vitrification as an alternative to achieve organ cryopreservation [2,3]. vitrification is the solidification of a substance with no crystallization, consisting in an increase of its viscosity and the formation of an amorphous solid (glass). for biological samples such as organs, the vitrification can be done by adding high concentrations of cpa before or during the cooling process. this high cpa concentrations are usually toxic, being the toxicity dependent on the temperature. therefore, a compromise between cpa concentration and temperature has to be reached. me2so is widely used in cryobiology as cpa and it is part of the composition of numerous cryoprotective solutions. in 1968, rasmussen studied the phase diagrams of the system me2so-water, showing that the no crystallization of the sample can be achieved by controlling two variables: the temperature of the system and the cpa concentration. while temperatura is easy to monitor, (e.g. thermocouple infrared thermometer, fluoroptic thermometer, etc…), the monitoring of the cpa concentration and distribution inside an organ is more complex. the present method is based on two cornerstones. one is the use of x-ray ct to monitor and control the cryoprotectant inside the organ during its perfusión and cooling. the second one is the use nanowarming of magnetic ice binding proteins. in our method, due to the low range of energy that we used, the attenuation depends mainly on the atomic number of the highest mass atom present, having proportional ct signals only to the me2so concentration, at any temperature. avoiding the recrystalization in organs by selective targeting of ice through magnetic ice-binding proteins can be highly beneficial. the elimination of ice is done by the combined use of magnetic particles and ice binding proteins, a complex that we will call magnetic ice binding proteins (mibp). ice is melted and re-solidified with the help of an alternating magnetic field pulse, acting on the mibp. then, with the organ free of ice, the rewarming is modelled by "standard" nano-warming. on the other hand, as an energy source, instead of coherent laser radiation, an alternating magnetic field (hundreds of khz) which is highly permeable to the organ can be used. the alternating magnetic field has recently been successfully used to achieve rapid warming of cryopreserved samples [13]. comsol multiphysics software (ac and dc modules coupled with the heat transfer module) were used to model this selective targeting of ice. the maxwell-garnet model was used for the complex relative permittivity. in conclusión: the toxicity of the cryoprotector is lower when the biological material is colder. the damage produced in the organ during the rewarming process can be reduced through a previous rewarming by using nanoparticles linked to ice binding proteins. vitrification of rat heart prove the possible cryopreservation of organs.rewarming of the vitrified rat hearts by using nanoparticles and magnetic ice binding particles for cleaning the ice during the cooling or before the rewarming, could be considered as alternative to the conventional methods.