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Safe transport of organs and tissues for transplants: technological innovation product validation method

Bartira de Aguiar Roza[1*], Sibele Maria Schuantes Paim[1], Renata Leite[1], Adriana Ferraz Carbonel[2], Murched Omar Taha[3], André Ibrahim David[3], José Maria Soares Junior[4], Manuel de Jesus Simões[2], Janine Schirmer[1*]

Brazil is a country with expressiveness and relevance in the organ and tissue donation and transplantation scenarios. Numerical indicators regarding the rate of transplants demonstrated this importance. During 2021, 23,929 cells, tissues, and organs transplants were performed[1].

However, despite this numerical indicator, the waiting list for transplantation is still lengthy. During the first semester of 2022, 51,674 people were registered waiting for the treatment, which often means a chance for continue living[2].

Due to the difference between the number of transplants and the number of people on the waiting list, strategies are developed to look for problems and failures in the cells, tissues, and organs donation and transplantation processes, as well as improvement opportunities. Regarding these strategies, it was identified that organs and tissues were lost ofdue to logistical problems. According to the Brazilian Association of Organ Transplantation (Associação Brasileira de Transplantes de Órgãos – ABTO), in 2022, 15% of the organs offered were not transplanted for various reasons. Some of these reasons were related to fragilities during the packaging for transport[2].

Currently, the organs are packaged in three primary packages and then in a thermal box filled with ice for transport[3]. Identification is done with labels standardized in current legislation[4], and the internal temperature is not controlled. Furthermore, the packaging route is not shared.

The problems with this type of transport are related to the lack of temperature control, causing the organs to freeze when in contact with the ice or, due to the thawing of the ice, the temperature increase. Both situations result in tissue death and, thus, there is not control over the quality of the transplanted organ.

Being faced with the identified problem, a group of researchers started to develop a package that would meet the requirements and safety criteria for this type of transport, including temperature control and industry 4.0 enabling technologies, that is, an interactive system with data collection and storage using cloud, and artificial intelligence[5].

The research idea as well as the development and production of this package arose from nurses' concern on the quality during their assistance to transplants. In their routines, nurses experienced and still experience the impact of these problems on the life of patients and on the health systems. The project is developed in two other public institutions and in a private one in the state of São Paulo, Brazil[5].

However, to ensure that the technological product is safe and widely used, a clinical validation method was developed. For this purpose, organs and ocular tissues obtained from Landrace line pigs (due to the similarity with humans' organs and ocular tissues) will be used in simulated organ extraction surgeries. Twelve experiments will be conducted, of which two pilot tests are used to improve the method and 10 experiments using the case-control method are adapted for clinical validation purpose.

Studies using this method aim to compare the individual's exposure to some factors that can trigger an outcome of interest. Normally, it is a retrospective study that aims to identify the existence of casual association between the factor's exposure and the disease under study[6,7]. In this case, for the technological product validation, the study's object is the new packaging that works differently from the packaging used in the Brazilian reality. Therefore, the main risk factor is the integrity maintenance of the organs and tissues transported.

[1]Universidade Federal de São Paulo, Escola Paulista de Enfermagem – São Paulo (SP), Brazil.
[2]Universidade Federal de São Paulo, Escola Paulista de Medicina, Department of Morphology and Genetics – São Paulo (SP), Brazil.
[3]Universidade Federal de São Paulo, Escola Paulista de Medicina, Discipline of Operative Technique and Experimental Surgery – São Paulo (SP), Brazil.
[4]Laboratório de Ginecologia Estrutural e Molecular - LIM 58 da Disciplina de Ginecologia, Departamento de Obstetrícia e Ginecologia, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo – São Paulo (SP), Brazil.
*Corresponding authors: bartira.roza@unifesp.br; schirmer.janine@unifesp.br
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To determine the package's capacity to maintain organs and tissues viable to transplant, operational analysis will be performed. Safety issues, temperature, transport conditions, ergonomics, histomorphology, and microbiology will be evaluated.

Data collection will be done following the standardized organ and tissue extraction process performed in humans. Anesthetic procedures in pigs will be carried out, followed by the removal of the heart, liver, pancreas, kidneys, and ocular globes. Then, organ perfusion, macroscopic analysis regarding the organs and tissues characteristics using an instrument made for this purpose, and, finally, samples collection for the histomorphological and histomorphometric analysis will be performed. Finally, packaging organs and tissues in primary packages with preservation solutions and in secondary packages for transport will be carried out in test (experimental package) and in the package already in use (control package) with ice.

Ground transport will be carried, and once returned to the surgical place, the same analyses described above will be performed. In addition, before and after transport, to compare microbiological growth, swabs will be collected in both packages using a protocol developed for this study (three collections at the bottom of the box, three in the top of the box, and three in the support for biological samples inside the box), totaling 18 samples each package.

Regarding the morphological analysis, it will present important data about the morphology of the transported organs and tissues. In this way, in the heart, the cardiac striated muscle tissue (cardiomyocytes), nuclei, intercalated disks, and the entire cardiac stroma will be evaluated. In the liver, central lobular vein, hepatocytes, portal space (branches of the portal vein and hepatic artery, respectively), bile ducts, lymphatic vessels, and nerves will be evaluated. In the pancreas (exocrine and endocrine portion), lobules, septa, and glands in the pancreatic stroma will be evaluated. In the kidney, glomeruli, proximal and distal convoluted tubules, and entire renal stroma will be evaluated. In the ocular globes, the cornea (dense modeled connective tissue), anterior and posterior epithelium, the sclera (dense non-modeled connective tissue), vascular tunic (uvea comprising the iris, choroid, and ciliary processes), and retina will be evaluated.

Thus, with these data, it is intended to see the tissue morphology and quantify it using specific software. This type of analysis is called histomorphometry, which constitutes the first step in carrying out the approach to new tissues. This analysis will allow to quantify and statistically show the comparison of organs and tissues between the two packages under test.

In addition, immunohistochemistry technique will be performed to search for cellular and tissue antigens in order to analyze proteins that participate in the cell death process, seeking to analyze the specific proteins that participate in cell proliferation and apoptosis in the evaluated organ[8,9].

Finally, the main purpose of this process is to guarantee the entry into the market of a new and safe innovative product to be used in the transport of organs and tissues for transplants. Therefore, reducing the loss of these organs caused by logistical and transport problems and, consequently, increasing the number of patients with access to this treatment and reducing the waiting period for an organ or tissue will all impact the lives of these people.

AUTHORS' CONTRIBUTIONS

BAR: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **SMSP:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **RL:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **AFC:** Methodology, Project administration, Supervision, Validation, Writing – original draft. **MOT:** Resources, Supervision. **AID:** Software, Validation, Visualization, Writing – original draft. **JMSJ:** Writing –original draft, Writing – review & editing. **MJS:** Writing – original draft, Visualization. **JS:** Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Project administration, Writing – original draft, Writing – review & editing.

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