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The impact of the International Atomic Energy Agency (IAEA) program on radiation and tissue banking in Brazil

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Abstract Until 2000, efforts into organising tissue banks in Brazil had not progressed far beyond small "in house" tissue storage repositories, usually annexed to Orthopaedic Surgery Services. Despite the professional entrepreneurship of those working as part time tissue bankers in such operations, best practices in tissue banking were not always followed due to the lack of regulatory standards, specialised training, adequate facilities and dedicated personnel. The Skin Bank of the Plastic Surgery Department of the Hospital das Clinicas of Sao Paulo, the single skin bank in Brazil, was not an exception. Since 1956, restricted and unpredictable amounts of skin allografts were stored under refrigeration for short periods under very limited quality controls. As in most "tissue banks" at that time in Brazil, medical and nursing staff worked on a volunteer and informal basis undergoing no specific training. IAEA supported the implementation of the tissue banking program in Brazil through the regional project RLA/7/009 "*Quality system for the production of irradiated sterilised grafts*" (1998–2000) and through two interregional projects INT/6/049 "*Interregional Centre of Excellence in Tissue Banking*", during the period 2002–2004 and INT/6/052 "*Improving the Quality of Production and Uses of Radiation Sterilised Tissue Grafts*", during the period 2002–2004. In 2001–2002, the first two years of operation of the HC-Tissue Bank, 53 skin transplants were carried out instead of the previous 4–5 a year. During this period, 75 individuals donated skin tissue, generating approximately 90,000 cm^2 of skin graft. The IAEA program were of great benefit to Brazilian tissue banking which has evolved from scattered make shift small operations to a well-established, high quality tissue banking scenario.

Keywords Brazil · Tissue banking · Radiation processing · Sterilisation · Allografts

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The early period

Since 1997, Federal Law No. 9.434 regulates organ donation. It basically states that every individual is a potential multi-organ donor, unless stated against in the identity card and/or in the driver's license. In

1998, an addendum to the law was adopted, suggesting family consent before organ procurement. The Federal Decree 2.268 from 1997 established the National Transplant System, by which the Ministry of Health is in charge of all procurement and disposition of organs in Brazil, assuring the minimum standards for donor selection and storage of organs. To expedite organs donations and procurement, a National Transplant Organisation has been established that supervises regional and local procurement teams, as well as gives the necessary credentials for a medical institution to actually perform organ procurement and transplantation.

The need of organised structures (tissue banks) dedicated to processing and long-term storage of human tissue for later transplantation was a consensus among those taking care of patients, such as extensively burned victims or bone tumour cases. Until 2000, efforts into organising such banks in Brazil had not progressed far beyond small "in house" tissue storage repositories, usually annexed to Orthopaedic Surgery Services. Despite the professional entrepreneurship of those working as part time tissue bankers in such operations, not always best practices in tissue banking were followed due to the lack of regulatory standards, specialised training, adequate facilities and dedicated personnel. Tissue access was mainly through living donors; access to multi-organ donors was sporadic. Tissue output was regulated by the tissue bank surgeon's specific needs and both production and distribution geared by internal needs. Tissue irradiation as a mean of terminal sterilisation was unknown and discard rates were significant.

The Skin Bank of the Plastic Surgery Department of the Hospital das Clinicas of Sao Paulo, the single skin bank in Brazil, was not an exception. Since 1956, restricted and unpredictable amounts of skin allografts were stored under refrigeration for short periods under very limited quality controls. As in most "tissue banks" at that time in Brazil, medical and nursing staff worked on a volunteer and informal basis undergoing no specific training. Despite the recognized life-saving benefits brought by the availability of allograft skin in the local Burns Unit, albeit in restricted quantities, there were no available resources to expand this program.

This explains the enthusiasm of the Plastic Surgery Department of the Hospital das Clinicas to join the group performing radiation-sterilisation of biomaterials at the Instituto de Pesquisas Energeticas e Nucleares (IPEN), a well-known institute developing nuclear energy research, into the Latin American program of the IAEA. This program proposed to assist, through training of personnel and provision of essential equipment, the establishment of tissue banks in the region, which would utilise ionising irradiation as means terminal sterilisation of tissue products.

The new tissue bank in the Hospital das Clinicas was organised with views of establishing the basis of a regional multi-tissue bank to be expanded in the future into a bio-engineered tissues centre. Despite the fact that there was a small skin bank functioning in the hospital for many years supplying tissue to the Burns Unit, and that local orthopaedic surgeons were familiar with allogeneic tissue transplantation from several sources, the initial challenge was to draw the support of hospital authorities to the project. Then to upgrade the existing facilities and to engage qualified dedicated personnel, so as to reach internationally accepted standards. Through funding from public and private sources, the Banco de Tecidos do Hospital das Clinicas a new area was refurbished to accommodate a facility within internationally acceptable standards which included an administration office, a preparation/ storage area and two processing rooms with quality controlled environment. The IAEA provided support through the donation of equipment, expert advice and training of dedicated personnel. The tissue bank was officially inaugurated in October 2000. By January 2001 it was fully operational as far as skin grafts production, introducing the concepts of skin processing in highly concentrated glycerol (>75%) and radiosterilisation in Brazil.

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The constitution of the current University of Sao Paulo-Hospital das Clinicas Tissue Bank generated a longstanding partnership between the Hospital das Clinicas one of the major medical centres in Sao Paulo, Brazil, affiliated to the University of Sao Paulo

Medical School and the Instituto de Pesquisas Energeticas e Nucleares (IPEN). As a result of this cooperation tissue processing is carried at the tissue bank and, when applicable, terminal sterilisation is performed at IPEN—CNEN/SP. Both institutions are also in the forefront of research in Brazil, enabling for new protocols in radiation-sterilisation to be established and approved by the Health Ministry.

The evolution of tissue banking activities and the impact of the IAEA program

In 2001–2002, the first two years of operation of the HC-Tissue Bank, 53 skin transplants were carried out instead of the previous 4–5 a year. During this period, 75 individuals donated skin tissue, generating approximately 68,750 cm^2 of skin graft. These grafts, most of them preserved in >75% glycerol were used in patients with extensive burns or other trauma in the Hospital das Clinicas, as well as in other medical facilities, both in Sao Paulo and throughout the country.

During the period of 2001–2006, the total number of skin donors was 152, generating approximately 153,000 cm^2 of processed skin, of this total 28,950 cm^2 were irradiated. Until 2006, the number of patients that receive the allograft skin was 146, using 146,500 cm^2 (Table 1).

In 2003, the HC-Tissue Bank also started to store cranial bones at −80°C to be used as autograft transplant or to research. Until 2006, 65 cranial bones were stored and 7 of them were transplanted.

In addition, tissue output has risen since, in both numbers and quality standards. The increasing demand for tissue had led to a new upgrade of the facility in 2006. It now has doubled its original area to include four processing rooms, an enlarged tissue preparation/storage area, and improved space for administration and quality controls.

Table 1 Human skin processed and distributed by HC—Tissue Bank

Year	Donors	Skin area donated (cm^2)	Receptors	Skin area transplanted (cm^2)
2001	42	38,500	20	25,300
2002	33	30,250	33	38,000
2003	19	21,800	25	23,800
2004	28	28,300	32	23,100
2005	23	26,500	24	26,800
2006	7	8,000	12	9,500
Total	152	153,350	146	146,500

In accordance with the commitment with IPEN to engage in new product research and the use of radiation sterilisation technology in tissue banking, a program on the effects of radiation sterilisation on glycerolized skin has been developed with favourable clinical results. Working protocols for future products such as lyophilised bone, acellular dermis and amniotic membrane are being developed. The tissue bank has also provided scientists with tissue samples to be used in biotechnology research, such as scaffolding for keratinocyte cultures in bioengineered tissue substitutes.

However, far more important than the increased production of high quality tissues, the conceptual changes in Brazilian tissue banking culture brought though the IAEA program deserves to be highlighted. Several individuals benefited from the direct contact with the excellent international tissue bank experts that visited Brazil for different training purposes. Each visit brought new insights in tissue banking at its best for those involved directly in the tissue bank operations.

Two professionals graduated in the Singapore and four in the Buenos Aires Regional Training Centres courses supported by IAEA. All remained involved in tissue banking, translating the acquired knowledge into higher operational standards at their own tissue banks, establishing new tissue bank operations and implementing national strategies and norms.

Visits to international highly standing tissue banks provided additional operational knowledge. This was a driving force to provide some individuals with the expertise to participate as consultants in the makings of the national muscle-skeletal and skin tissue banking standards issued in 2002.

The highly regarded standing of the IAEA in the Brazilian political and scientific community added value to the efforts of tissue bankers to call attention to the need of increased professional and public awareness about tissue donation and the need to support non for profit tissue banking in Brazil.

The Hospital das Clinicas Tissue Bank became a national reference as far as physical plant and operational standards. This has provided the opportunity to help designing and overseeing the

operational standards of other national tissue banks, such as the recently inaugurated Skin Bank in Porto Alegre (2006).

An important network amongst national tissue banks was established through sharing of acquired knowledge through the IAEA program. The Banco de Tecidos do Hospital das Clinicas representatives became very active in national consultations. Regional networking developed, culminating with the establishment of the Latin American Tissue Banking Association (ALaBaT), when a Brazilian member directed linked to the program became the Vice President and later, President.

The impact of the IAEA program in tissue banking activities in Brazil can be summarised as follows:

(a) Increased skills amongst professionals involved in the processing and radiosterilisation of tissues, with a direct impact in the quality of the tissue banking industry.
(b) Establishment of a tissue bank, which remains as a gold standard in national tissue banking.
(c) Increase in public and professional awareness about tissue donation.
(d) Tissue donation and tissue banking became part of the Brazilian Health Ministry agenda.
(e) Expansion of the use of nuclear energy in Brazil, with the introduction of radiosterilisation of tissues.
(f) Increased production of high quality tissue products.

The current situation of tissue banking activities

The original Hospital das Clinicas Tissue Bank developed within the IAEA program, remains in the forefront of tissue banking industry driving new initiatives. The improved facility will allow for the incorporation of the Eye Bank, which will fulfil its original multi-tissue concept. The expectations are that this initiative will have a national impact and other mergers will follow once the benefits of multi tasking and production cost sharing become understood by the professional tissue banking community. Operational standards for muscle-skeletal and skin banking have been introduced by ANVISA, the national regulatory body, where the IAEA Standards have been utilised as a guideline.

With these clear GMP practices, other tissue banks have improved their operational standards. Smaller operations have closed down and through the National Transplant Coordination there is a strong impulse to establish a centrally manned network for tissue distribution. In contrast to 2000, there are five high standard Muscle-Skeletal Banks, two Cardiac Tissue and two Skin Banks fully operational in Brazil. Although exact figures are still unavailable, tissue output certainly is increasing, in both numbers and quality.

There are still some important hurdles to be overcome. Financial resources to take existing tissue banks to a next level of operational excellence still are limited. Most tissue banks are based on cost-recovery systems and the pricing and reimbursement through the public health system is lacking in efficiency. That drives the distribution to the private system, establishing a potential conflict of interest.

To overcome these factors the Brazilian Health Ministry is building an electronic network system to oversee tissue banks stocks and distribution of tissues. This networking system would ensure a fair distribution of tissues on a first-come first-served basis, making the best out of available tissue nationwide and allowing for immediate reimbursement of operational costs for the tissue banks. This faster financial turnover should provide resources to better fund the activity and needed quality assurance improvements.

Despite a strong and highly funded public health organ transplantation program, there are no clear incentives for the tissue banking program which is reflected in the access to a limited numbers of tissue donors. Demand for tissue products clearly surpasses availability. Public health authorities recognise this deficit; however, although there are strong efforts to increase rates amongst multi-organ donors, the evident need to increase public and professional awareness remains a challenge.

A recent initiative to establish a dedicated retrieval room within the Forensic Medicine Department at the University of Sao Paulo led by the HC-Tissue Bank may enable access to cardiac arrested donors and set another model for the tissue banking community.

Funding for further scientific developments and protocols also remains in the realm of restricted public funding and grants. These certainly do not encompass new product development costs.

There is no doubt that the IAEA program was of great benefit to Brazilian tissue banking which has evolved from scattered make shift small operations to a well-established, high quality tissue banking scenario. There is still much room for growth and improvement where the successful results of the IAEA program have to be maintained through strong national engagement and further international support.