

1 THE INTERNATIONAL ATOMIC ENERGY AGENCY (IAEA) PROGRAMME IN RADIATION AND TISSUE BANKING: PAST AND PRESENT

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1. The Early Period

The IAEA has gained more experience and success than any other international organisation in establishing Tissue Banks in developing countries and applying ionizing radiation for sterilising tissue grafts used in transplant surgery (in orthopaedic reconstruction, treatment for cancer, trauma and high velocity impact damage), the treatment of burns, leprosy and intractable skin wounds, and pressure sore ulcers.

This extensive programme has its origins in an IAEA Expert group meeting in the Joliot Curie Radiobiology Institute in Budapest around 1971, when it was resolved that there were advantages to be gained by using ionizing radiations to sterilise human and animal tissue. Yet for the early years, these interests

were pursued under a broad cover of the sterilisation of medical products. The first declaration of the IAEA's official move into this field came with the 1974 Symposium in Bombay on "Sterilisation of Medical Products and Biological Tissues". The first vehicle used by IAEA was the Research Coordination Programme. Interested parties were encouraged to collaborate to study the effects of radiation on tissues. The outcome of this work was the IAEA Advisory Group Meeting held in Athens in 1976 on "The Effects of Sterilising Radiation Doses upon the Antigenic Properties of Proteins and Biological Tissues". The Proceedings of the meeting have been published (Phillips *et al.*, 1978). In retrospect, it can now be realized how historic this meeting was; with pioneers in the broader subject of Tissue Banking participating: Gary E. Friedlander, Kenneth W. Sell, D. Michael Strong, K. Ostrowski, Sandor Pellet, Rudolph Klen, A. Dziedic-Goclawska, Pe Khin and Nicholas Triantafyllou.

Thereafter, the programme gained momentum. Meetings under the auspices of IAEA were held in the Republic of Korea (1978) and Czechoslovakia (1981). The experience of the Eastern European countries was particularly helpful over this early period. The first truly Tissue-Banking contract (BUR/7/004) provided by IAEA emerged shortly afterwards, and in March 1983 a Tissue Bank was established in Burma (now Myanmar).

From the mid-1980's the name "Tissue Banking" began to appear in official IAEA titles of programmes. Among the first was Sri Lanka where the late Dr. Hudson Silva had already established his famous Sri Lanka Eye Donation Society. Thailand thereafter played a major role in stimulating the programme in Asia and the Pacific Region through the contribution of Dr. Y. Vajjaradul. The first Regional Workshop was held in Bangkok in November 1989 under the auspices of the IAEA Regional Coordination Agreement (RCA). To coincide with this meeting was the foundation of the Asia Pacific Surgical Tissue Banking Association, of which Dr. Vajjaradul was the first Secretary General.

It was the RCA programme, which delivered the necessary impetus and financial support, with Dr. John Easy being the RCA Coordinator who supplied the push over a ten-year period. The other pioneering Technical Officers at IAEA were Dr. Ramen Mukherjee and Dr. Vitomir Markovic. It was their support and vision that initiated the development of the first Training Curriculum in Radiation and Tissue Banking, using distance learning anywhere in the world. More detail about the historical development is given in Phillips and Strong (1997 and 1999), Phillips and Tatsuzaki (1998), Phillips (1999), Phillips (2000) and Phillips and Morales (2002).

2. Economic and Health Care Impact

In all, some 30 countries have subsequently been involved (but not all funded) in this initiative: in Asia/Pacific Region: Australia, Bangladesh, China, India, Indonesia, Japan, Republic of Korea, Malaysia, Pakistan, Philippines, Singapore, Sri Lanka, Thailand and Viet Nam; in Latin America: Argentina, Brazil, Chile, Cuba, Mexico, Peru and Uruguay; in Africa and Middle East: Algeria, Jordan, Libya, Zambia and Iraq and in Europe: Greece, Poland, Turkey and Slovakia. All these countries are using radiation sterilisation as the method of choice. Experts from Australia, Europe, Japan and USA have assisted the IAEA Radiation and Tissue Banking Programme.

In the countries involved with the IAEA Radiation and Tissue Banking Programme, as experience has been gained, the growth had been exponential. To the end of the year 2000, more than 220,000 tissue allografts have been produced and used clinically. Taking the mean value of the cost levied by Tissue Banks in the USA and Europe, as a re-charge for the processing, the value of these grafts can be placed at US\$51,768,553.

The total expenditure associated with the IAEA Radiation and Tissue Banking Programme over the same period was US\$6,313,335, which includes a training cost of US\$2,036,034. Not only does these provide a benefit in health care to these

countries but also avoid the costly importation of grafts into the country. In Mexico, for example, when a US\$400 graft is imported from USA, the cost to the patient is at least US\$3,000, due to value added taxes, import, agent, hospital charges, etc. It costs US\$10,000 to import a whole femur from USA into the Republic of Korea. The following tables summarise the main outcomes of the IAEA Radiation and Tissue Banking Programme in general, and in the Latin America region in particular.

The graft production over the period 1988–end 2000 in 16 countries for which data has been reported is the following (Table 1):

Table 1. Graft production and cost benefits.

Cancellous bone	Massive bone allografts	Skin and Amnion	Others*
69,195	8,588	96,645	50,278

*Pig skin, dura mater, demineralised bone, xenografts, pericardium, tendon, ligaments, and fascia. The total graft production is 222,580, valued at US\$51,768,553 (at mean European and USA Tissue Bank prices).

In Latin America, the IAEA supported the formation of 7 Tissue Banks and trained 66 Doctors, Tissue Bank Operators and Nurses. Table 2 shows the distribution of the trainees who have set out to establish Tissue Banks and used the country nuclear center to carry out the radiation sterilisation of their grafts. It summarises the position at the end of 2001.

The main benefit, however, is undoubtedly the improvement in health care in the individual countries. There exist major problems in the use of autografts, which is grafts taken from the patient and then transferred to another site during surgery, as already noted. Also, the available amount of autograft bone, particularly in child or infants, is limited. The second lesion offers a site for potential infection, which is particularly relevant in a developing country. Skin and amnion offer immediate cover

Table 2. Catalysing the start up of new Tissue Banks in Latin America.

Country	Number on National Training Course	Attended 1 year Training Course	Number of Fellowship Training	Number of New Tissue Banks	Date when joined IAEA Programme
Argentina	3	16	7	11	1993
Brazil		4		6	1998
Chile		4	2	4	1998
Cuba	10	5	6	10	1994
Mexico		6	3	4	1996
Peru		2	5	1	1994
Uruguay		2		1	2001
Total	13	39	23	37	

Note: Initial total Tissue Banks in the region is 7.

for burns, wounds or leprosy lesions, which can promote healing, prevent fluid and energy loss and the introduction of infections.

Another major advantage of the IAEA Programme in these countries is the exposure that surgeons get to the newer methods of using allografts and creating a cultural change in their approach to surgical treatment in their country. In Western countries, the use of such grafts is now routine, and more than one million are used world-wide. The perceived need in a developing country is not always apparent, but as the technology is introduced, the health benefits become clear. When this occurs, the graft supply is far from sufficient. The IAEA Programme has inspired this revolution in many countries and the growth henceforth will be exponential.

Finally, it is not possible to measure the benefits for giving more than 220,000 people restored limbs, prevention of amputation, repair of fractures and spinal defects, or to treat burnt children and people who have been burnt or suffer from diseases like leprosy, or paraplegics who are vulnerable to pressure sores.

This is the true measure of the benefits of the IAEA Programme.

3. Innovative Training

Distance learning training for tissue banking operators, managers and doctors within the IAEA Radiation and Tissue Banking Programme started in 1995. Initiated in the Asia and Pacific Region, with the support of international experts, the Singapore Government and the National University of Singapore, the first comprehensive IAEA/NUS Curriculum in Radiation and Tissue Banking was produced. It is now a tangible asset.

This Curriculum, now available in English, Spanish and Korean, is an unique vehicle for delivering training of tissue bank operators, managers and doctors worldwide. The University Diploma extends over one year, starting with a two week face-to-face contact in Singapore or Buenos Aires, is the first available anywhere in the world. In Asia/Pacific, Latin America, Africa and Europe, 296 tissue bank operators, managers and doctors have been trained under the IAEA Radiation and Tissue Banking Programme, out of which 65 have been successful graduated in the University of Singapore and 9 at the University of Buenos Aires. For the 81 trainees from 18 countries who attained the University Diploma level, the total cost was US\$557,117 compared with US\$972,000 in the UK for the same level course, using conventional training methods.

4. The On-going Programme

A Global Programme has been identified, which will place all activities within an inter-regional and regional structure. There is now an unified management and evaluation system for all activities. The inter-regional programme provides the basic expert and technical services, which can then be transferred to Latin America, Asia/Pacific and Africa Regions for implementation through the regional projects. There has been recently requests from a group of European countries, including Ukraine

and Russia, which indicate a more active participation of the European region in the IAEA Programme. The IAEA Programme will ensure that all tissue banks have access to the latest international standards, and supported with documentation to enable them to mount an effective public awareness and tissue production programmes to promote health and economic benefits within their region and country.

The activities will all be designed to ensure better public acceptance of the benefits of radiation sterilised tissue grafts and ensure that the same uniform international standards are being used throughout Asia/Pacific, Africa, Latin America and eventually the European region. The key initiatives will be:

- (a) The IAEA International Standards for Tissue Bank: Presently there is a great deal of variation. Expert and regional groups will review the present adopted USA and European practice and the planned activities will ensure that these, when adopted, are compatible with regional circumstances.
- (b) The IAEA Code of Practice for the Radiation Sterilisation of Biological Tissues. No international body has undertaken this important function, which is within the IAEA's technical competence. This Code of Practice will then be introduced into the regions for practical evaluation.
- (c) The IAEA Handbook for Public and Professional Awareness: Public and professional awareness is the major obstacle to even further extension of the use of radiation sterilised grafts in individual countries. Education is needed at all levels. Documentation to assist workshops and national programmes will be prepared and adapted to the regions in several languages.
- (d) Internet training: Internet training will be introduced for all "Radiation and Tissue Banking" training courses all over the world. This is a logical extension and will build upon the IAEA Distance Learning Programmes now being used. The resources of the multi-media curriculum and its recent update, needs to be exploited in this way to give full benefits to IAEA. Already the educational methods and technical

needs have been analysed, and as a result an implementation strategy agreed.

In April 2002 the first International Training Course for Tissue Bank Operators was held in Singapore with the participation of 23 students from 13 countries of Africa, Latin America, Asia and Europe. The Tissue Bank in Singapore will become the International Center for Training Tissue Bank Operators when a Memorandum of Understanding is signed with the National University of Singapore. Another training course at the regional level will be held in 2002 in Buenos Aires for the Latin American countries. Eight participants will be accepted from 7 countries. It is expected that a Memorandum of Understanding will be signed between the IAEA and the National Atomic Energy Commission of Argentina in the following months to allow the establishment of a Regional Training Center for tissue bank operators in the country for the Latin America Region.

A Memorandum of Understanding was signed in May this year with the Musculo-skeletal Transplant Foundation (MTF) in the USA to promote the co-operation with the IAEA in the field of tissue banking, in particular in the area of training medical doctors and transplant coordinators.

The establishment of a Homepage on the Internet for the IAEA Programme was finalised in 2002 (www.tissuebanking.org).

Areas for co-operation between the IAEA and WHO have been identified and a letter of intention have been prepared and submitted for approval to the competent authorities in both organisations.

5. Benefits to Developed Countries

Before the IAEA Programme started using radiation to sterilise tissues, the situation elsewhere in the world was very mixed. There were misconceptions about the benefits of using this technology, which are considerable, such as:

- No significant temperature, physical and chemical changes are

induced which influence the required function of the tissues.

- The high penetration enables the bulk of the hard or soft tissues to be sterilised in final packaged form. The systematic use of radiation sterilisation in final packaging reduces the cost of investment by approximately 80% compared with alternative methods.
- The effect is instantaneous and simultaneous for the whole target. The process control is precise and can be applied accurately to achieve sterility. Irradiation time is the only variable to achieve a sterility assurance level of 10^{-6} .

A series of cases, particularly in the USA, where infections were transmitted through tissues, which had not been end-sterilised, drew fresh attention to the experience of the IAEA Radiation and Tissue Banking Programme. Now at least half of the grafts in the USA are either being sterilised or decontaminated using radiation. The method is mandatory in Austria and widely practised in UK, Germany, Belgium, Slovakia, Poland and France.

At a conservative estimate, it can be demonstrated that at least 600,000 tissues grafts in developed countries are now being annually radiation sterilised directly as a result of the IAEA Programme, through a type of reverse educational transfer to developed countries. Experts from developed countries are supporting the IAEA Programme. This is a confirmation that the benefits of collaboration between developed and developing countries are not all one-way.

6. References

- PHILLIPS, G.O., TALLENTIRE, A. and TRIANTAFYLOU, N. (eds.) (1978). *Radiation Sterilisation of Irradiated Tissues and their Potential Uses*, The North East Wales Institute, Wales, UK.
- PHILLIPS, G.O. and STRONG, D.M. (1997 and 1999). The Contribution of the International Atomic Energy Agency to Tissue Banking, *American Association of Tissue Banks: Tissue and Cell*

Report, 1997, **4**(1), 5–10, and *Advances in Tissue Banking* (ed. G.O. Phillips), **3**(1999), 357–397.

PHILLIPS, G.O. and TATSUZAKI, H. (1998). The Tissue Banking Programme supported by the International Atomic Energy Agency (IAEA), *Transfusion Today*, **37** (December), 24–25.

PHILLIPS, G.O. (1999). Tissue Banking in the Asia Pacific Region, *Advances in Tissue Banking* (ed. G.O. Phillips), **3**(1999), 399–402.

PHILLIPS, G.O. (2000). The future role of the International Atomic Energy Authority (IAEA) in Tissue Banking, *Cell and Tissue Banking*, **1**, 27–40.

PHILLIPS, G.O. and MORALES, J. (2002). Catalysts of Better Health Care: Medical Tissue Banks Bring Multiple Benefits to Countries, *International Atomic Energy Agency Bulletin*, **44**, 17–20.