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A Review of the International Atomic Energy Agency (IAEA) Code of Practice for the Radiation Sterilisation of Tissue Allografts

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Abstract

The code of practice adopted by the IAEA sets out the main requirements to ensure that the radiation sterilisation of tissues produces sterilised tissue allografts suitable for safe clinical use.

The IAEA main contribution to the process of tissue sterilisation is the development of the guideline in using radiation for tissue. Sterilising tissue grafts using ionising radiation which is being used in many countries, offers a clear advantage in terms of safety compared with other sterilisation techniques for health care products and medical devices.

Keywords: Ionising radiation; Sterilisation of tissues; Code of practice, IAEA; Radiation dose

Introduction

The International Atomic Energy Agency (IAEA) program on radiation and tissue banking has been previously described in detail by Phillips and Morales [1,2]. It is important to knowledge that during the period 1960s-1970s, the ionising radiation technique was used in several countries mainly for the sterilisation of health care products and medical devices [3].

However, in the 1980s, the IAEA started to consider the possibility to use the ionising radiation technique for the sterilisation of human and animal tissues, as the terminal processing step undertaken following strict guidelines for donor selection and graft processing, all conducted within an overall quality system for which strict operational standards were specified [4].

During the 1980s, 1990s and 2000s, the IAEA vigorously promoted the use of the ionising radiation technique for tissue sterilisation in its Member States under more than 36 national, regional and interregional technical cooperation projects in 31 countries in Asia and the Pacific, Latin American, Africa and Eastern European regions, involving more than 70 tissue banks. More than US$ 7 million were allocated to support the implementation of these projects.

During the last three decades, the IAEA has demonstrated that the sterilisation of tissues using the ionising radiation technique offers a clear advantage in terms of safety compared with other sterilisation techniques now in use in different countries [5]. Fortunately, most tissues, including bone, skin and amnion, can be treated with ionising radiation to kill microorganisms, without affecting their functionality. The use of the ionising radiation technique, in the case of skin and amnion, require the presence of a cryoprotectant. At the same time, it is important to stress that the use of this sterilisation technique significantly reduces the risk of transferring communicable diseases to the receptor.

Other methods of tissue sterilisation using heat and chemicals have also been practised in some countries for a long period of time. It has been demonstrated that the sterilisation of tissues using heat and steam techniques could damage the tissue's biological and physical properties or composition, whilst sterilising it with ethylene oxide gas leaves toxic residues that warrant quarantine period before the sterile products can be used [6][1]. At the same time, it has been proved in practice that a radiation dose of 25 kGy or lower has no damage to the tissues or this damage is minimal, and is particularly safe from the environmental point of view as it does not leave any chemical residues in the sterilised tissue [1].

Under the quality system proposed by the IAEA, sterilisation methods used for the sterilisation of tissues must be validated. In some countries it is even a legal duty [1]. Validation of the chosen sterilisation method gives a documented record on the effectiveness of inactivating or eliminating microorganisms. The use of the ionising radiation technique promoted by the IAEA program has proved to be an effective sterilisation technique of tissues, if specific conditions are met and the proper radiation dose given.

In 2007, the IAEA published a code of practice entitled "Radiation Sterilisation of Tissues Allografts: Requirements for Validation and Routine Control" for guiding tissue bankers in the proper use of ionising radiation technique for sterilisation of tissue allografts [7].

The aim of this paper is to briefly identify missing elements that are relevant to tissue bank using the ionising radiation technique for sterilisation purposes and are not included in the current version of the Code. However, it is important to stress that the paper does not have the intention of reviewing the methodology used for the calculation of the radiation dose.

[1]After the quarantine period the toxic residues disappears and the tissue can be used safely.

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Main reasons for the preparation of the IAEA Code of Practice

The first question that needs to be considered is the following: Why the IAEA decided to prepare this document? The IAEA Code of Practice contains the main requirements that need to be observed by all tissue banks in order to ensure that a radiation sterilisation dose selected for sterilising a specific tissue is correctly validated or substantiated before the dose can be used for routine sterilisation of these tissues.

Prior to 2007, the document ISO 11137 [8] was used as a reference to select and validate radiation doses. However, this document was prepared as a guide for the sterilisation of health care products and medical devices, which have different technical characteristics than human and/or animal tissues. In addition, the use of Methods 1 and 2 of the ISO 11137 [8] required a high number of samples and this was very difficult to have in the case of tissues, due to the fact that the availability of processed tissues per production batch is always very limited and usually in various sizes and shapes.

Method 1 included in the current version of the IAEA Code of Practice, allows tissue bankers to use less samples to validate the sterilisation dose to be given to the tissues. However, this assumption should be substantiated from the scientific point of view and demonstrated in practice. The current version of the IAEA Code of Practice does not give enough scientific probe that this assumption is the correct one in all cases and under all situations.

In addition, the different formulae included in the methodology used by the IAEA Code of Practice for the determination of the sterilisation dose should be clearly demonstrated that they are the correct ones from the mathematical point of view. This is something not very clear in the methodology included in the current version of the Code. These studies should be carried by a group of experts selected by the IAEA under specific guidelines to be elaborated by this specialised organisation.

It is important to single out that before the IAEA started to promote the use of the ionising radiation technique for the sterilisation of tissues, only a few IAEA Member States had used the ionising radiation technique to sterilise tissues, while others preferred to use other techniques for the same purpose. There were also some misconceptions about the benefits of using the ionising radiation technique for the sterilisation of tissues within several IAEA Member States [1].

Most of these States were not aware while some were not convinced that using the ionising radiation technique to sterilise tissues, under certain conditions and using the appropriate radiation dose, no significant changes in temperature, physical and chemical properties occur, which could influence the required function of the tissues, and that the high penetration of the radiation enables the bulk of the hard or soft tissues to be sterilised in their final packaging.

The process control is precise whereby exposure time is the only variable that needs to be controlled, therefore, the required radiation dose can be delivered accurately to attain the predetermined Sterility Assurance Level (SAL) of 10^{-6} [1,6].

Why have several IAEA Member States changed their opinion about the use of the ionising radiation technique for tissues sterilisation purpose? These misconceptions changed significantly after a series of incidents occurred particularly in the USA, where infections were transmitted through transplanted tissues, which had not been end-sterilised [1]. This situation drew attention afresh to the experience of the IAEA in the use of the ionising radiation technique for tissue sterilisation within its program on radiation and tissue banking. As result of this change, now at least half of the grafts in the USA are either being sterilised or de-contaminated using the ionising radiation technique. Gamma radiation kills microorganisms by attacking the DNA molecule, which results in the prevention of cellular division and, consequently, the propagation of life.

It is important to note also that the use of the ionising radiation technique for tissue sterilisation is widely used in other countries with good results including Argentina[2], Belgium, Brazil, Cuba, China, France, Germany, Indonesia, Malaysia, Mexico, Slovakia, Poland, Peru, Thailand, Singapore, Uruguay and the UK. Worldwide, conservative estimate of about 600,000 or more tissues grafts in industrialised countries are sterilised annually using radiation [8].

Tissue banks operating in countries that were using the ionising radiation technique for the sterilisation of tissues, particularly in Asia and the Pacific and in the Latin American regions, used a target dose of 25 kGy. They tried to follow ISO 11137 [7] and ISO/TR 13409 [9] to validate the process [2]. The use of these documents for tissue sterilisation purposes provoked a great concern to the IAEA in its effort to promote the ionising radiation technique. Why does this cause concern? It is important to be aware that population (type and distribution) of microorganisms and levels of bioburden in human and/or animal tissues are different than the ones that can be found in health care products and medical devices, where the levels of microbial contamination are usually low and the tissues are relatively not uniform in size and density [7].

To overcome this problem the IAEA decided, in 2001, to prepare a technical document to be used specifically for tissue sterilisation purposes using the ionising radiation technique. This document adopted similar principles as applied to the radiation sterilisation of health care products and medical devices, but at the same time tried to take into account the special features associated with viral transmission, biological tissues and also the physical and chemical properties, which distinguish tissues from industrially produced health care products and medical devices [2].

However, and despite all efforts made by the IAEA's experts to differentiate both documents as much as possible, the current text of the IAEA Code of Practice followed to some extent the ISO document used for the sterilisation of health care products and medical devices.

For this reason, after some years of using the Code in several IAEA Member States the current version of the Code should be revised taking into account the different proposals included in the present paper, among other specific proposals that could be presented during the revision process or even before. One of the issues not included in the current version of the Code is what to do if the tissue is contaminated with virus, a type of contamination that normally does not exist in heath care products and medical devices.

In addition, tissue allografts are not products of commercial manufacturing processes whereby the number of tissue products per batch is limited and this situation resulted in limited or insufficient number of samples for validation process.

[2]Argentina has used ionising radiation technique for sterilisation of tissue allografts following ISO/TR 13409 [9] before 2000 for sterilisation dose determination [10].

In 2006, ISO 11137 [12] was adopted in order to replace the ISO 11137 [8]. Methods 1 and 2 of the ISO 11137 [12] as before allow selection of doses other than 25 kGy. The new VD_{max} approach included in the new ISO document, depending on bioburden of the product, offers the validation of 15 kGy (VD_{max15} Method) as well as the substantiation of 25 kGy (VD_{max25} Method).

The revision of the IAEA Code of Practice is, therefore, timely following major revision of the ISO 11137 [8] document used as reference for the preparation of the current version of the Code.

The appropriate radiation dose for tissues sterilisation

The IAEA Code of Practice recommends a standards radiation target dose of 25 kGy for the sterilisation of tissues. However, there are different points of views regarding the level of the radiation dose to be given to certain types of human and/or animal tissues for sterilisation purpose under certain conditions. For example, the application of gamma irradiation for terminal sterilisation of bone allograft is well accepted, but the dose of gamma radiation is still controversial. For example, in a survey of 36 American tissue banks, the dose of radiation used for sterilisation ranged from 10 to 35 kGy [13]. Other opinions on the level of the radiation dose to be given for sterilisation purposes can be found in [14].

It is important to stress, according to Dziedzic- Goclawska [15], the selection of radiation dose for a specific tissue for sterilisation purposes must be a compromise between dose that is high enough to inactivate the tissue microbial load and low enough to preserve important biological properties of the tissue allografts.

Two methods are available in the IAEA Code of Practice for the determination of a radiation dose for sterilisation purpose. The main limitation of these methods is that the selection of the radiation dose is based on statistical approaches that have been established for the sterilisation of health care products and medical devices as previously described in the following documents: ISO 11137 [8], ISO/TR 13409 [9], ISO/TR 15844 [16] and AAMI TIR-27 [17].

However, all of the above documents are now obsolete and were replaced by ISO 11137 [12]. The current version of the IAEA Code of Practice does not include any of the main changes introduced in ISO 11137 [12]. This is one of the reasons for which the current version of the Code should be revised as soon as possible.

As mentioned earlier, tissues are produced in a limited number and with physical and biological characteristics that are very different from health care products and medical devices. In addition, tissue allografts are not uniform in size, shape and density. The low number of uniform samples available in human tissues is, without any doubt, a limiting factor that should be taken into account during a validation of a radiation dose for tissue sterilisation.

The Code must consider giving more examples on how the number of samples required for validation work can be met and how this limited number of samples can substantiate the radiation dose selected. This limitation and how it can be handled should be clearly explained in a revised text of the IAEA Code of Practice to be prepared in the future, because it may have an important influence in the results obtained. The examples and the explanations given in the Annex of the current version of the Code are not enough.

A brief summary of the different opinions regarding the level of the radiation dose given to certain types of human tissues for sterilisation purpose are described in the following paragraphs, with the intention to demonstrate the need of revising the recommended dose included in the current version of the Code.

According to some experts, if the tissue microbial distribution follows a Standard Distribution of Resistance (SDR) of ISO 11137, the tissue bank may choose either to establish new doses or to substantiate a maximal verification dose or VD_{max} of 25 kGy for microbial levels up to 1000 colony forming units (cfu) per allograft product. Alternatively, for the SDR and other microbial distribution, specific sterilisation doses may be validated depending on the bioburden level and radiation resistance (D_{10} values) of the constituent microorganisms [14].

However, it is important to note that if the resistance and population of microorganisms are unknown and cannot be measured directly, then the worst case scenario should be assumed. In this case, it is recommended that the highest D_{10} value for the resistant microorganism be used for setting the sterilisation dose.

In Poland, for example, a dose of 35 kGy was recommended in this case, which they believed could provide better assurance of sterility for tissue allografts than the commonly used dose of 25 kGy [15]. Other countries supported the use of radiation up to 50 kGy for the sterilisation of frozen tissues. Others use a lower dose [2,14].

After lowering the bioburden to less than 10^3 cfu per tissue, a radiation dose lower than 25 kGy can be used for sterilisation purpose without adverse consequences [7]. This is especially important for soft tissue to minimise radiation damage keeping the functional roles of the tissue. As Method 1 of the ISO requires large numbers of samples for the dose validation, VD_{max} approach of the new ISO offers simpler method with less number of samples required i.e. Method VD_{max15} and VD_{max25}. Bioburden of less than 1.5 cfu per tissue is required for substantiating a radiation dose of 15 kGy according to VD_{max15} [18].

Taking into account the different approaches described in the above paragraphs and with the objective to find a scientific conclusion on the level of the radiation dose to be given to specific tissues for sterilisation purpose, the IAEA should support the realisation of scientific studies to be carried out by a group of selected experts in the field of radiation sterilisation, in order to identify the adequate level of the radiation dose to be applied to a group of selected tissues for sterilisation purposes. At the same time, these studies should identify which are the necessary changes to be introduced in the methodology used by the current version of the Code, with the aim that it can be used without any doubt.

Other missing elements

Due to the importance of the correct use of the IAEA Code of Practice by those using the ionising radiation technique for tissue sterilisation, some additional elements to the ones already mentioned in the previous paragraphs, should be considered during the revision of the current version of this document.

Objective and scope

The IAEA Code of Practice sets out the main requirements to ensure that the use of the ionising radiation technique for tissue sterilisation produces standardised sterile tissue allografts with SAL 10^{-6} suitable for clinical use. There should be no doubt that in order to provide sterilised tissues of reliable quality, good practices must be observed by all tissue bank staff starting from strict donor screening, retrieval of tissues, testing, processing, sterilisation, storage and delivery of processed tissues. The revised text of the current version of the IAEA Code of Practice should emphasise these important elements.

The Code should be able to accommodate any needs which arise from new and advanced technologies in tissue banking which provide improvement in tissue quality, other than already addressed in the document. For example, new processes such as improved washing procedures and advanced technologies, as well as cell and tissue engineering, could be developed by tissue banks in the coming years. It is important that the Code could take advantages of the existence of new technologies in the field of tissue banking and in the field of radiation for sterilisation purposes. For this reason, it is advisable that the Code be revised, at least every five years, in order to keep abreast with any new development in the field of radiation of tissues for sterilisation purposes and in tissue banking.

Personnel

The IAEA Code of Practice stressed that "the responsibility for the validation and routine control for sterilisation by irradiation, including tissue donor selection, tissue retrieval, processing, preservation, sterilisation and storage, shall be assigned to qualified personnel" [7]. There is nothing in the Code about the importance that the personnel in the irradiation facility should be fully trained. For this reason, the following idea should be included in a new version of the IAEA Code of Practice: It is equally important that personnel working in the irradiation facility in charge of the sterilisation of tissues are fully trained, particularly in the use of the Code, in order to have the necessary skill and qualification to deliver accurate radiation dose during verification and routine sterilisation activities.

Validation of pre-sterilisation processes

An essential step in the overall processing of tissues is the rigorous donor selection to eliminate specific disease transmissions. However, once the tissue is procured, there are four main sources of potential contamination for the tissues after it has entered the tissue bank: a) Processing areas; b) Tissue bank staff; c) Ancillary material; and d) Cross-contamination from tissues of different donors. Specific measures should be adopted within a tissue bank to avoid the contamination of the tissue during processing. However, it is important to stress that some of these measures are related specifically with the use of certain techniques for the sterilisation of tissues.

In case that the ionising radiation technique is used with sterilisation purpose, then irradiation facilities staff in charge of the sterilisation of the tissues should be trained to apply the IAEA Code of Practice in the most effective and secure manner.

The IAEA Code of Practice emphasises the need to carry out certain serological tests which are clearly described in the current version of this document. However, other tests may be required by statutory regulations in some countries or when specific infections are identified. In using such laboratory-based tests to provide additional assurance that tissues are free of transmissible diseases, due consideration should be given to the detection limits of such tests. It should, therefore, be verified that the combination of processing, preservation and irradiation is capable of eliminating or reducing contamination to an acceptable level in the procured tissue. This aspect should be included in any future revised text of the current version of the IAEA Code of Practice to be prepared in the coming years.

Validation of the sterilisation process

The validation of the process used for the sterilisation of tissues should be performed by adequate measurements of the absorbed radiation dose set a priori and required to achieve the specified SAL. In addition to proper dosimetry systems, it is advisable to use radiation-sensitive indicators as stated in ISO 11137 [12] Part 3.

Emphasis is given by the IAEA Code of Practice on the factors which affect the ability of the sterilisation process to demonstrate that an appropriate SAL can be achieved with low numbers of tissue allografts, which may have more variability in the types and levels of microbial contamination than could be found in health care products and medical devices, and which may also be more variable in size and shape.

Several factors not only affect the effectiveness in the use of the ionising radiation technique for the sterilisation of tissues, but can also modify microbial sensitivity to ionising sterilisation. One of these factors is bioburden. The lower the bioburden is, the more effective the process will be.

For this reason and, in accordance with ISO 11137 [12]:

a) Careful screening and selection of donors should be performed.

b) Tissue from more than one donor should not be pooled during retrieval, processing or storage to avoid cross-contamination between tissue donors.

c) All the procedures should be carried out under aseptic or as clean conditions as possible.

d) Instruments and equipment used during retrieval and processing should be sterilised to avoid contamination, when necessary.

e) After retrieval, tissues should be processed and preserved as soon as possible and subsequently sterilised.

f) If immediate processing and preservation are not possible, then tissue should be stored temporarily at low temperature or frozen to prevent proliferation of microorganisms and to diminish the action of proteolytic enzymes before sterilisation.

g) Personnel should be trained properly on how to work in clean / aseptic area.

h) Good Manufacturing Practice / GMP should be implemented in all steps of the processing process.

These elements are advisable to be clearly mentioned in any future revised text of the current version of the IAEA Code of Practice, in order to ensure the maximum effectiveness in the use of the ionising radiation technique for sterilisation purposes.

Improving the IAEA Code of Practice

The current version of the IAEA Code of Practice, as a fundamental document to guide the proper use of ionising radiation technique for tissue sterilisation, can be improved further by taking into account the above mentioned elements. During the revision of the Code, the following considerations should be properly addressed:

a) The Code follows too closely old ISO documents used for the sterilisation of health care products and medical devices and does not include the changes introduced in document ISO 11137 [12].

b) The whole issue of viral contamination and how to deal with important types of contamination is missing[3].

c) It is important that experts in the use of the ionising radiation technique study carefully how the Code could deal properly

[3]It is important to stress the following: To include virus inactivation in the new version of the IAEA Code of Practice, it is necessary to do further studies of radiation resistance of virus and its posterior statistic exhaustive treatment.

with new emerging viral diseases caused by new type of viruses such as AH1N1, H5N1, dengue and West Nile Virus (WNV) and viruses in window period, if necessary. Screening methods and possibility to eliminate those unknown virus are advisable to be discussed thoroughly in order to see if they can be included in a future revised version of the current text of the IAEA Code of Practice, by adding D_{10} value of viruses and recommended combined treatment of radiation with processing or washing methods [19-21].

d) The experience gained by different IAEA Member States in the provisional use of the IAEA Code of Practice are not included in the current version of this document [21-23].

e) The latest development in the field of sterilisation using ionising radiation technique is not addressed in the current text of the IAEA Code of Practice, for example, ISO VD_{max} approach for low dose irradiation [12].

Taking into account all elements mentioned in this paper, the revision of the current version of the IAEA Code of Practice is strongly advised. The revision process should address these issues, among others, particularly a set of recommended radiation doses to be given to specific tissues for sterilisation purpose, without affecting its biological characteristics, prepared on the basis of different studies carried out by competent institutions located in several countries.

A comprehensive IAEA Code of Practice is extremely important for the tissue banking community and should become a handbook for radiation facilities in assisting their customers that require tissue sterilisation using the ionising radiation technique.

Conclusion

The IAEA Code of Practice has undoubtedly assisted tissue banks in many countries in the application of ionising radiation technique as a routine treatment for tissue sterilisation.

Taking into account the importance of the use of the IAEA Code of Practice as a reference by tissue banks and radiation facilities in relation with the use of the ionising radiation technique for sterilisation of tissues, it would be very important that this Code be revised and updated periodically every five years. The purpose of the revision is the incorporation of the latest developments in the field of radiation sterilisation and the experience gained by those IAEA Member States that are using the ionising radiation technique for the purpose of sterilisation of tissue allografts.

The revised Code will complement other documents, standards and guidelines on radiation sterilisation of medical products and pharmaceuticals already in use in several countries.

References

1. Phillips GO, Morales Pedraza J (2003) The International Atomic Energy Agency (IAEA) program in radiation and tissue banking: Past, present and future. Cell Tissue Bank 4: 69-76.
2. Morales Pedraza J (2006) The IAEA program on tissue banking. A successful program for developing countries. Cell Tissue Bank 7: 237- 258.
3. IAEA (1998,2007) Thematic planning reports on tissue banking. IAEA, Vienna, Austria.
4. Loty B (2005) IAEA International Standards for Tissue Banks; In: Sterilisation of Tissues using Ionising Radiations. Woodhead Publishing and CRC Press. England.
5. Yusof N (2001) Effects of Radiation on Microorganisms-Mechanism of Radiation Sterilisation; Ed. Nather A; The Scientific Basis of Tissue Transplantation. World Scientific, Singapore.
6. Yusof N, Hilmy N (2007) Need for Radiation Sterilisation of Tissue Grafts; In: Radiation in Tissue Banking. World Scientific, Singapore.
7. IAEA (2007) Radiation Sterilisation of Tissue Allografts: Requirements for Validation and Routine Control – A Code of Practice. STI/PUN/1307, IAEA, Vienna, Austria.
8. ISO 11137 (1995) Sterilisation of health care products - Requirements for validation and routine control - Radiation sterilization. International Organisation for Standardisation. Geneva, Switzerland.
9. ISO/TR 13409 (1996) Sterilisation of health care products - Radiation sterilisation - Substations of 25 kGy as sterilisation dose for small or infrequent production batches. International Organisation for Standardisation. Geneva, Switzerland.
10. Silberman F, Kairiyama E (2000) Radiation sterilisation and the surgical use of bone allografts in Argentina; Advances in Tissue Banking. World Scientific 4: 27-38.
11. Phillips GO, Morales J (2002) Catalysts for a bigger medical attention, tissue banks doctors offer multiple benefits to countries. Bulletin of the IAEA, IAEA, Vienna, Austria.
12. ISO 11137 (2006) Sterilisation of Health Care Products- Radiation - Part 2: Establishing the Sterilisation Dose; International Organisation for Standardisation. Geneva,Switzerland.
13. Vangsness CT, Triffon M, Joyce MJ, Moore TM (1996) Soft tissue for allograft reconstruction of the human knee: a survey of the American Association of Tissue Banks. Am J Sports Med 24: 230-234.
14. Nguyen H, Morgan DA, Forwood MR (2007) Sterilisation of allograft bone: is 25 kGy the gold standard for gamma irradiation? Cell Tissue Banking 8: 81-91.
15. Dziedzic-Goclawska A(2000) The Application of Ionising Radiation to Sterilise Connective Tissue Allografts. In: Radiation and Tissue Banking. World Scientific. Singapore.
16. ISO /TR 15844 (1998) Sterilisation of Health Care Products – Radiation Sterilisation - Selection of Sterilisation Dose for a Single Production Batch. International Organization for Standardisation. Geneva, Switzerland.
17. AAMI Technical Information Report (TIR)-27 (2001) Sterilization of Health Care Products- Radiation Sterilisation – Substantiation of 25 kGy as a Sterilisation Dose. McLean. Virginia, USA.
18. Yusof N (2007) Radiation Sterilisation Dose Establishment for Tissue Grafts – Dose Setting and Dose Validation; In: Radiation in Tissue Banking. World Scientific. Singapore.
19. Pruss A, Von Versen R, Pauli G (2005) Viruses and their Relevance for Gamma Irradiation Sterilisation of Allogenic Tissue Transplant; In: Sterilisation of Tissues using Ionising Radiations. Woodhead Publishing and CRC Press. England.
20. Hilmy N, Pandansari P (2007) New Emerging Diseases caused by Viruses and Prion, How radiation can overcome them; In: Radiation in Tissue Banking. World Scientific. Singapore.
21. Hilmy N, Febrida A, Basril A (2007) Experiences in using the IAEA Code of Practice for the Radiation Sterilisation of Tissue Allografts. J Rad Phy Chem 76: 1751-1755.
22. Strong DM (2005) Effects of Radiation on the Integrity and Functionality of Soft Tissue. Current Situation: Cartilage, Heart Valve, Tendons and Other Tissues. Changes with Increasing Dose/Dose Limits. In: Sterilisation of Tissues Using Ionising Radiations. Woodhead Publishing and CRC Press. England.
23. Yusof N (2005) Is the irradiation dose of 25kGy enough to sterilise tissue grafts? In: Bone Grafts and Bone Substitutes – Basic Science and Clinical Applications. World Scientific. Singapore.