COMPUTATIONAL SIMULATIONS IN MEDICAL RADIATION A NEW APPROACH TO IMPROVE THERAPY

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Abstract

This article deals with computational simulations in medical radiation through stochastic and deterministic methods. The major goal is to show the power of the computational modeling in dealing with applied medical irradiation describing some examples and results from computational models. Brachytherapy modeling will be exemplified by the RADPLAN code, which does a radiotherapy planning for a distribution of sealed radioactive sources. Modeling a restenosis treatment based on neutron irradiation will be a second example. Microdosimetry's simulations provide insights in how metastasis can be treated by systemic radiotherapy. Dosimetry's evaluation from Samarium incorporated seeds is also addressed. Computational modeling in Sinovectomy gives a general broad example of how radiation modeling may apply in health. Also, simulations in a proposed ^{252}Cf - ^{235}U irradiation facility will be addressed. To the validation of the theoretical results, a phantom's construction and how it is used to experimental dosimetry is discussed. Preliminary studies in vitro of the deleterious effects of the irradiation helps in validation. Those examples illustrate the power of computer simulations in dealing with complex problems such as radiation therapy.

Keywords*: computational simulations, cancer therapy, and medical radiation*

1. INTRODUCTION

This article deals with the computational simulations in medical radiation based on stochastic and deterministic methods, looking for new approaches for improving radiotherapy. The major goal is to show the power of the computational modeling in dealing with applied medical irradiation through some examples and results.

The cancer therapy based on nuclear particle irradiation is the main focus, considering neutron, electron and photon nuclear particles generated by external focus beam or internal radioisotopes - sealed or systemic. A radiation planning for Brachytherapy - technique in which sealed sources are placed as close as possible to the tumor - has been proposed. Small sealed micro sources filled with I-125, Cs-137, Ir-192, Au-198, and Cf-252 radionuclides are implanted,

whose irradiation neutralizes cancerous cells in tumor. Computational simulation is the main tool to provide safety and accuracy in the cancer treatment. Computational modeling helps in predicting physical variables such as absorbed dose, particle flux, current, absorbed energy, per transition or per tissue volume and mass. Stochastic and deterministic models to evaluate particle transport in matter was used in a code namely RADPLAN to obtain 3D-dimensional dose rates into the human body. Techniques such as Cf-252 Brachytherapy has been studied and it is the main focus of the research. Those simulations may provide data to support the first application of this therapy in South America. Cf-252 Brachytherapy coupled with neutron capture therapy is an idealized therapy. Simulations on this matter may provide insights to improve cancer therapy.

In some circumstance, Radiation also improves health to the hearth. Irradiation reduces the phenomena of high proliferation of abnormal epithelial cells in the artery wall, namely restenosis. A new treatment namely EPRIN for treating restenosis will be one of the examples of how insights from computational simulations may bring benefits to human heath.

Sinosvectomia - a rheumatoid chronic joint disease and the way of how radioisotopes will neutralized it is also addressed. A common fact of all those techniques is that the computational model deals with nuclear particle in biologic matter based on stochastic or deterministic approaches.

2. A BRIEF ON THE NUCLEAR PARTICLE TRANSPORT SIMULATIONS

2.1 Stochastic Approach

Monte Carlo technique represents a numeric computational process that looks for the reproduction of a physical real event. The expect value of one, or a group of random variables, will replace one, or more, unknown physical entity. This value is represented by the average value taken from various independent samples, following by a statistic uncertainty. The random processes based on the possible most exact simulations of the physical processes mimic the nuclear particle behavior in matter, generating infinity number of individual histories. The physical laws, the mathematical representations of those laws, and the experimental nuclear data are the tools for those simulations. Nuclear codes such as MCNP, EGS, GIANT, EPIC, and nuclear data files such as ENDF, JEF, among others, are the main computational tools for the stochastic approaches of the nuclear particle phenomena in matter. MCNP - Monte Carlo N-Particle Transport Code System, for photons, takes account coherent and incoherent scattering, fluorescent emission after photoelectric absorption, pair production absorption with local emission of annihilation radiation, and Bremsstrahlung. A continuous slowing down model is used for electron transport.

2.2 Deterministic Approach

In contrast, deterministic approach for modeling nuclear particle transport implies to solve the Boltzmman equation to understand the non electric particles behavior - such as neutron and gamma rays; or, the Folck Plank equation when electric charge are present - such as electrons, protons, and charged nuclei. The non homogeneous and complex human body geometry, in which is found high absorbed, moderators, voids, textured tissues - such as lungs, creates serious conditions to solve such equations. Simplifications and sophisticated techniques such as Finite Element may be addressed to operate the space domain. Added to multigroup technique for

energy, and finite differences for angular, the computational model solve the Boltzmman equation and can predict particle behavior in human body.

3. COMPUTATIONAL MODELING IN MÉDICAL RADIATION - SOME EXAMPLES AND RESULTS

This section describes some of the on going studies in computational modeling from the medical radiation research group at Nuclear Science and Technique graduate course from UFMG.

3.1 Brachytherapy Modeling - RADPLAN code

RADPLAN code provides the 3D-isodose distribution in the irradiated volume generated by a 3D-dimensional radioisotope source distribution. The present code shows the isodoses curves drawing over a digitized medical image - X-ray, CT, or MRI images (Costa & Campos, 2000). A friendly interface is in development to give the physician ability to operate it without training. In the first tests, real data from clinical radiation planning were used and the greater divergence between doses from the code was 2%.

The main goal is to evaluate in an optimized way the internal dosimetry in the patients submitted to radioactive implants, with seeds or wires of I-125, Ir-192, Au-198, Cs-137, as well as Cf-252 micro sources with or without radiosensitizers. The deterministic approach is based on the model developed by Atomic Energy of Canada which evaluates exposition in air and corrects it to dose in tissue. This correction is done by a polynomial expression that accounts the events of absorption and scattering in water and tissues, whose coefficients were experimentally obtained first by Meisberger . Stochastic approach is based on a Voxel model developed in MCNP.

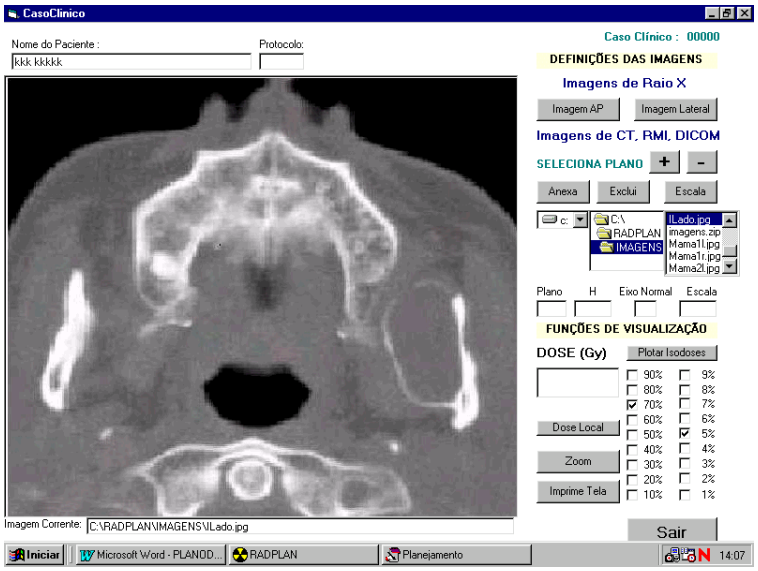

Figure 1 – Image view of an output from RADPLAN

3.2 Modeling Restenosis treatment based on neutron irradiation

Restenosis, i.e. a vascular re-narrowing process, results from angioplasty. Preclinical studies point out that radiation can bring benefits on reduction of restenosis incidence. A new method to irradiate the region “in locus” namely EPRIN - Electron-Photon Radiotherapy Induced by

Neutrons to treat restenosis has been proposed. EPRIN, similar to NCT, is a non-invasive binary procedure (Campos, 2000). At the first, special wires interlaced with the stents are implanted together on a permanent fashion. Those wires are madding of a non-radioactive nuclide that gathers the condition of having a high absorption cross section, type (n,γ). At the second, when it is required, a collimated beam of neutrons illuminates the outside target region. The instantaneous photon-electron irradiation "in locus" starts with the neutron presence, transmuting the stable nuclide in the wire to a stable product with reduced mass, releasing energy. Theoretical results were obtained through the photon-neutron transport code MCNP4A. Various nuclides have been tested. A relevant result for a unique cadmium wire into a 10mm diameter vessel located 3 cm deep from surface shows a physical dose deposition of $7.08.10^{-11}$Gy/external-neutron beam. Therefore, for an external neutron fluence of $3.2.10^{10}$ n/cm^2 illuminating a 7.06 cm^2 disc source -6 cm diameter, a total gamma physical dose of 16 Gy will be generated on the artery wall. A flux of 2,5 10^7 n.cm^{-2}.sec^{-1} applied for 3 minutes will give the required treatment dose. The total physical gamma dose is 70% less if the wire is made of an Eu-151 uncovered in a metal basis; therefore, a 6 minutes will be enough to generate the required dose. Those results illustrate the feasibility of treating restenosis with the electron-photon irradiation Brachytherapy induced by a non-invasive external beam. A spatial physical dose distribution of the dose rates obtained by a Voxel model has been found for eight cadmium's microwires placed close to an artery wall. Figure 2 depicts some results.

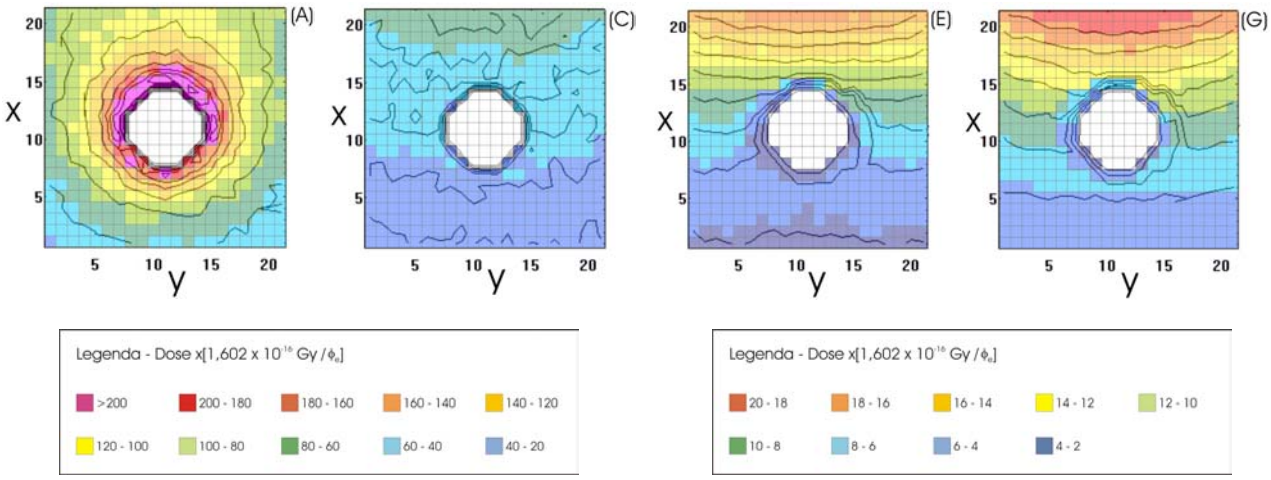

Figure 2 - Photon dose from neutron capture reactions in the artery region (a) transversal section at plane z in origin with stent loaded (c) without stent.

3.3 Microdosimetry's Simulations on Systemic Radiotherapy

The metastases are the major reason for cancer death. The radiotherapy systemic proposes the prescription of systemic radiopharmac that, through its many ways of affinity with the cancerous cells, will concentrate on the tumor and in its metastasis, generating a physical dose namely control dose for the colony propagation. The present section holds the goal of modeling the cancerous lesions with approximately 10^3 – 10^4 cells from a lung metastasis with radiopharmac uptake (Mendes & Campos, 2001). The radioisotope uptake can be in three compartments: nucleus, cytoplasm or interstice, dependent on the molecular affinity. The present computational evaluation is necessary otherwise the control dose cannot be estimated on those undetectable lesions. Important parameters must be addressed, such as: i) number and geometry of the cells; ii)

histological and morphological features; iii) affinity of the drug to the cellular lineage type; iv) time and way of biologic and physical decay of the radioisotope; v) nuclear interactions with the tissue and manners of energy deposition, traces and range of the emitted particles; vi) radiopharmac concentrations extra and intra cellular – nuclear and cytoplasm.

The model represents a group of 9261 viable cells forming a cube of 210μm of side. The size and the density of each cellular compartment were based on the average of the same ones for lung human cells. A cube of 18μm size length and 0.9g/cm^3 density models the cytoplasm. The cell nucleus was defined as a 6 μm diameter sphere with 1.1 g/cm^3 density. All individual cells are apart by 2μm, creating a cellular interstice, with 1.0 g/cm^3 density. The tumoral mass is embedding into a cube of 10 mm side filled with equivalent tissue. The nucleus, the cytoplasm and the interstice are composed with material that preserves the percentage of Carbon, Hydrogen, Oxygen, Nitrogen, Calcium, Potassium, Sodium, Chlorine, and Sulfur from existent match in the lung tissue.

Three types of radiopharmac uptake is assumed: cytoplasm, nuclear, and interstice, exclusively. For instance, for cytoplasm uptake, nuclear particles was emitted obeying the In-111 decay yields and type incorporated by the pharmac, in all the cytoplasms. For each uptake-type the dose and the energy deposition were evaluated in all the compartments due to primary electrons and photons, and its secondary particles, considering the tracks, energy transfer, interactions-type, and energy deposition among compartments. Some results are summarized in tables 1, in which total deposited energy, in MeV [code *F08], is presented for a generic pattern cell. The pattern cell is in the middle of the colony of 10^4 cells.

The primary electrons generate absorbed doses, on the distinct compartments, 20-100 times superiors to those values appraised for the primary photons. Indeed, in spite of the electrons hold the lower part of the total exothermic energy released by the decay, they provide the larger doses in the compartments. The reasons are due to the short track and range of the electrons in the matter, compared with photons that escape easily from the colony in great majority.

Table 1 – Energy deposited in the compartments of the pattern cell, in MeV, with radioisotope uptake in the nucleus, in the cytoplasm and in the cellular interstice, [code *F08], normalized per In-111 decay.

PARTICLE EMITTED BY RADIOISOTOPE	Photon			ELECTRON		
	UPTAKEN			UPTAKEN		
ENERGY DEPOSITION (MeV)	**NUCLEUS**	**Cytoplasm**	**INTERSTICE**	**NUCLEUS**	**CYTOPLASM**	**INTERSTICE**
Nucleus	1.22E-10 ±0.03	9.73E-11 ±0.03	8.98E-11 ±0.04	3.39E-07 ±0.0002	9.86E-09 ±0.004	4.44E-13 ±0.37
Cytoplasm	3.30E-09 ±0.01	3.31E-09 ±0.01	3,24.E-09 ±0.01	2,13E-07 ±0.0009	4,88E-07 ±0.0003	2,11E-09 ±0.003
Interstice	8,82E-09 ±0.01	8,83E-09 ±0.01	8,74E-09 ±0.01	4,36E-09 ±0.01	5,87E-08 ±0.0016	5,35E-07 ±0.0004

3.4 Dosimetric evaluations of implant seeds.

The development of radioactive biocompatible and biodegradable implant seeds is in progress in order to extend the combat of cancer. The biodegradable seeds incorporate in its structure a radioisotope with a physical haft-live inferior to the biodegradation period. The procedures of implants are similar to those used in the permanent interstitial Brachytherapy, but in this case, applying biodegradable material compatible with the biological medium. The first goal is to incorporate Samarium into vitreous matrices obtained from sol-gel processing, impregnated with

Calcium (Roberto, Pereira, and Campos, 2001). Activation of the seeds and processing animal implants in similar conditions found in humans are in progress. Preliminaries results provided by computational simulations indicate that the absorbed dose are generated by beta rays from Sm-145. Computational model shows that a suitable sets of seeds, implanted in an adequate spatial distribution, provides a total dose from gamma and beta particles enough to control a tumor.

3.5 Computational modeling in Sinovectomy

Arthritis is a cause of suffering of a large number of people. It has a difficult diagnostic and treatment. The sinovectomy with radioactive material is a less invasive treatment having precise and well-established indications. Beta emitters are applied linked to a macro aggregate, whose goal is to destroy the inflammation process caused by the arthritis, reestablishing the normal function of the articulation. It increases the quality of life of the patient. We propose to make a Disprosium-165 and Samarium-145 aggregates, activate it with neutrons, and make qualitative studies in vitro and in vivo (Lima & Campos, 2001). The hypothesis that the macro aggregate is held into the joints a period of time enough to generate the adequate control dose is in progress by cyntilographic images and computational dose models. Dosimetric evaluation is done from simulations in MCNP code based on a Voxels geometric model. It reproduces the material and shape of the joints. Some results are present in figure 3.

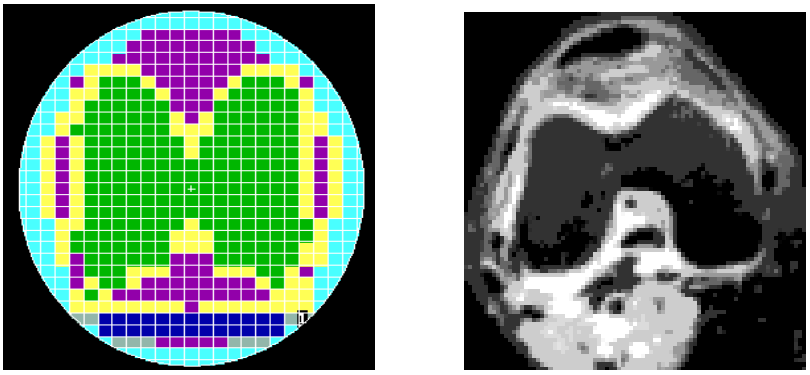

Figure 3 - Image view of an arbitrary section of the joint and the Voxel model

3.6 The proposed 252Cf - 235U Irradiation Facility

This section presents a cheap and simple irradiation facility that is able to deliver a good-quality epithermal neutron beam with low background of fast neutrons and gamma rays for applying in Neutron Capture Therapies (Costa H. & Campos, 2001). The proposed facility is composed of a set of ^{252}Cf sources coupled with special systems of moderator, collimators, filters and shielding. A geometric and material-choice optimization is made in order to maximize the epithermal neutron flux and minimize the fast neutron and gamma ray doses in the irradiation port. Monte Carlo N-Particle transport code – MCNP is used to estimate and optimize the main geometrical and material-choice parameters of the moderators, collimators, filters and shielding systems. The irradiation port is able to deliver an epithermal neutron flux at in the range of 4 eV up to 40 keV in a forward directional neutron current. In order to increase the intensity of the epithermal neutron flux in the beam port, a configuration loaded with ^{252}Cf-^{235}U is proposed in a subcritical neutronic fashion. This configuration presents an additional fuel fissile mass ^{235}U coupled with the ^{252}Cf neutron sources. In can deliver epithermal neutron flux up to 10^8n/cm^2.s

with low background of fast neutrons and gamma rays comparable with the figure-of-merits of the beam ports of the *MITR-II*, *BMRR* and *Petten* facility, presented in literature. The present facility may give opportunity to other groups to continue their work in BNCT. A mixed field of neutrons and gamma rays is created from the fission of ^{252}Cf isotope and the disintegration of the fission products, approaching 6.9 x10^{10} n/s and 3.96 x10^{11} gamma-rays/s. These sources have a radial distribution on the half height of the irradiator embed in cylinder heavy water moderator. The optimal radius is 15 cm for the source distribution and 5 cm for the central aluminum canal. External to the moderator tank of D_2O, a 15 cm thick bismuth shielding attenuates the undesirable gamma rays emitted from the own ^{252}Cf source and helps the neutron reflection on the walls. A thin sheet of lithium fluoride (enriched to 93% of ^{6}Li) is introduced between the D_2O moderator and the aluminum. The aluminum and LiF filters are placed in order to reduce the influence of the fast and thermal neutrons in the therapeutic beam. Collimators of bismuth and lithiated polyethylene (containing 45 wt% of lithium carbonate enriched to 93% in ^{6}Li) makes the neutron and gamma ray flux distributions centered in a cylinder irradiation port of 20 cm diameter. The ^{252}Cf-^{235}U configuration, embed on the D_2O moderator, presents two concentric cylindrical sheets of fissile fuel placed near the ^{252}Cf neutron sources. The total ^{235}U mass contained in this configuration is close to 1.75 Kg. The optimal configuration for the ^{252}Cf irradiator was obtained from various simulations using MCNP4A for several three-dimension geometries of moderator, collimators, filters and shielding systems, applying materials like Pb, Bi, C, Al, LiF, ^{6}Li, ^{10}B, S, Fe, Si, H_2O, D_2O, lithiated polyethylene, high density concrete, air and the homogenized alloy of UZrH (20% enriched to ^{235}U). The neutron and gamma ray spectra emerging on the central aluminum canal for the various mediums and for its geometric dimensions were evaluated in all calculations. The nuclear data libraries ENDL-85 and ENDF/B-VI were used for the MCNP continuous-energy simulations. The ^{252}Cf O_2 neutrons sources emit neutrons with energy between 1.4 up to 8.5 MeV, according to the spectrum of the ^{252}Cf neutrons source produced by the Amersham Corporation.[7] Gamma rays with energy in the range between 0.5 and 6.5 MeV emitted due to the fission of the ^{252}Cf isotope and the decay of its fission products were considered in the transport of photons exclusively. The criticality calculations of the proposed high flux ^{252}Cf-^{235}U irradiator were also computed in MCNP. The k_{eff} multiplication factor was estimated over 300 cycles, counting 1500 particles per cycle.

The major neutronic characteristics of the epithermal neutron beams, found in the literature, and estimated for the irradiation port of the proposed ^{252}Cf irradiators are tabulated in Table 1. The mixed configuration of ^{252}Cf-^{235}U presents an epithermal neutron flux up to 10^{8}n/cm^2.s achieving an amplification factor of 9.8 for epithermal neutrons in relation to the previous configuration without fuel, maintaining the low rates of fast neutron and gamma ray doses, and the directivity factor of the therapeutic beam. The criticality factor, k_{eff}, for this mixed configuration was estimated to 0.95885 ± 0.00131, keeping the irradiator facility in subcritical condition. The power of the central core with the k_{eff} at 0.95885 0.00131 is 0.1kWatts.

Table 1 - Major parameters of the epithermal neutrons beam ports applied to NCT in *MIT*, *BNL*, and *Petten*, and those of the proposed ^{252}Cf and ^{252}Cf-^{235}U irradiator

Reactor	ϕ_{epi} [n/cm^2.s]	$D_f/\phi_{ep\,i}$[Gy.cm^2/n]	D_f [cGy/h]	D_γ/ϕ_{ep}[Gy.cm^2/n]	D_γ [cGy/h]	**J/ϕ**
BMRR	1.8 x10^{9}	4.3 x10^{-13}	2.8 x10^{2}	1.3 x10^{-13}	8.4 x10^{1}	0.67
MITR-II	2 x10^{8}	13 x10^{-13}	9.4 x10^{1}	14 x10^{-13}	1.0 x10^{2}	0.55
Petten	3.3 x10^{8}	10.4 x10^{-13}	1.2 x10^{2}	8.4 x10^{-13}	1.0 x10^{2}	>0.8
^{252}Cf + 1.75 Kg ^{235}U	1.1 x10^{8}	32 x10^{-13}	1.3 x10^{2}	20 x10^{-13}	7.9 x10^{1}	0.998
^{252}Cf Irradiator	1.1 x10^{7}	31 x10^{-13}	1.2 x10^{1}	16 x10^{-13}	6.49	0.98

Both configurations of the proposed irradiator, ^{252}Cf and ^{252}Cf -^{235}U, present reasonable epithermal neutron spectra with low background of fast neutrons and gamma rays. It suggests a suitable use of the spontaneous fission ^{252}Cf neutron sources coupled with ^{235}U to the assembly of neutron irradiators. In spite of the low neutrons intensities obtained in the proposed ^{252}Cf irradiator configuration, this configuration already represents a good, safe and cheap neutron source to be applied in low-dose-rate neutron capture therapies. It may be applied in a fractionated treatment planed in various sections. The proposed configuration of a ^{252}Cf-^{235}U epithermal neutron facility has the drawback of the constant presence of the fissile fuel and its fission products. However the subcriticality and the expected simple procedures of maintenance and operation provide an attractive alternative as an epithermal neutron source. The ^{252}Cf-^{235}U and ^{252}Cf epithermal neutron facilities seem a good efficient neutron source able to be applied to neutron capture therapies in hospitals. Heat transfer analysis and final neutronic evaluations have been proposed for future work. Also, safe considerations for the fissile fuel coupled with ^{252}Cf source, toxicity, and analysis of costs for construction, operation and maintenance of both the proposed ^{252}Cf configurations are required in order to certify its viability on neutron capture therapies.

4. APPROACHING NEW ALTERNATIVE RADIOTHERAPIES

Computational modeling is the first tool for predicting the total dose, among other variables, in order to approach a new radiation therapy. Radiobiological research must also be done to provide information from the real biological response. Also, experiments must be performed to certify and calibrate the theoretical models. This section describes some work in progress that holds the goal of validation.

4.1 A Head and Neck Phantom for Experimental Dosimetry

The assembly of a head and neck phantom is in progress for development of experimental and theoretical studies involving the transport of photon and neutron particles (Andrade & Campos, 2001). The goal is that the phantom maintains the equivalence of the nuclear particle interactions with the human anatomy. The materials have equivalent properties to the tissue and bone, preserving the original anatomy. The placement of several nuclear detectors will allow experimental measures. It will collect experimental data form the particle flux and dose, taken in different protocols such as Brachytherapy and Teletherapy. The hypothesis is that the neutronic behavior in the phantom will be equivalent in a human head, providing the experimental evaluation of dose in several internal vital anatomic positions. The experimental data will be used later on to validate the theoretical models. The phantom has as base a human skull, donated by the Department of Morphology, Institute of Biological Sciences of UFMG. The measures of bony thickness of the cranium were taken previously. Equivalent tissue covers the skull. Solid state - TLD's, proportional detectors, or gold and cadmium foils will be used to collection the nuclear measures. Interstitial tubes are also being left in the molds for entrance and exit of the radioactive micro sources. The neck will be reconstructed with a resin equivalent tissue, preserving the intracavitary areas. Images from Computerized Tomography (CT), conventional Ray-X and Magnetic Resonance will be taken to check the anatomy. After the construction and verification, it will be used in internal dosimetry, making use of an afterloading procedure. The experimental measurements will be used for calibration of the deterministic and stochastic computational

models. The phenomenon of neutron transport in such a complex geometrically and heterogeneous area, as the head and neck, is totally unknown. The necessary quantification of this phenomenon is very important for the success of controlling head and neck tumors by neutron Brachytherapy.

4.2 In vitro studies of the deleterious effects of the radiotherapies

Studies of the deleterious effects induced by ionizing radiation are essential since the requirements of knowledge in the exactly biological response to a certain treatment. This biological response is quantified by the value RBE. It comes to multiply the physical dose obtained by the computational models. This response depends on several factors, besides of the particle type and energy involved in the radiotherapy. Tests in vitro will produce essential information for obtaining the RBE. Studies of the deleterious effects in glandular tissue: salivary gland tumors (mucoepidermoide carcinoma), mammary glandular tumors, and prostate tumors, comparative to the photon and neutron irradiation, are in progress (Andrade et al, 2001). Results preliminaries showed a high resistance of MDAMB-231 cancerous cells of breast tumor. Viability curves are being obtained of the lineages MDAMB231, HEC, HeLa, and leukocytes. Studies of cellular apoptose in irradiated cells are in progress. Apoptose means a programmed cellular death. It is a morphologic involution associated to the physiologic death of the cell. The apoptose is induced by radiation. Future tests will compare the deleterious effects of these lineages irradiated with Co-60, Cs-137 and Cf-252 (mixed field). The chosen techniques are the MTT assay to obtain the viability curves, as well as techniques of molecular biology at the level of the identification of the DNA breaks from gelagarose.

When the tumor cells are irradiated, the resulting interactions cannot produce differences that one can obviously observe such as in the characteristic of the cells or effects as intense as the cellular death in little hours. The changes that are in the cell will depend on a combination of factors, that determine the probability of cellular survival in response to a given radiation dose. Many factors can affect the cell response as the sensibility to the radiation, capacity of cellular repair and the mitoses capability of the lineage. The detection of the possible chromosome's aberrations in the cells, before and after irradiation, will give a sensitive analysis of the radiation.

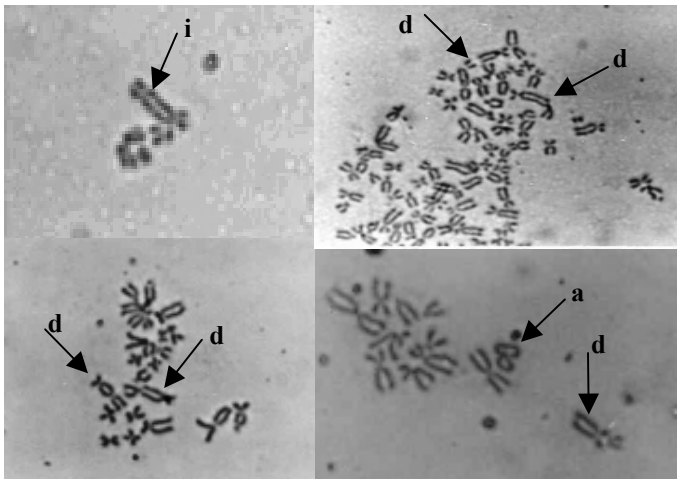

Figure 4 - Pictures of the chromosomes, colored with orceína. A - inverted chromosome (i). B - chromosome dicentric (di) and terminal deletion (dt). C - chromosomes dicentric (di). D - Anelament (a) and chromosome dicentric (di). 400x.

Cells submitted to 5Gy of Co-60 shows aberrations on chromosomes, easily identifiable, being most of the type dicentric. The dose level is function of the number of observed aberrations (Silva & Campos, 2001).

5. CONCLUSION

Dealing with human health, pre-clinical information is essential before any idealization of clinical trials. Thus, the mathematical and computational supports are clearly identified as important technique to be added to the area of radiation therapy. This article provided examples and results that showed a good support to medical radiation.

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