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Summary Report of Consultants' Meeting

Nuclear Data of Charged-Particle Interactions for Medical Therapy Applications

IAEA Headquarters, Vienna, Austria
20 – 22 November 2006

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January 2007

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Abstract

A summary is given of a Consultants' Meeting assembled to assess the viability of a new IAEA Co-ordinated Research Project (CRP) on *Charged-Particle Interaction Data for Radiotherapy*. The need for a programme to compile and evaluate charged-particle nuclear data for therapeutic applications was strongly agreed. Both the technical discussions and the expected outcomes of such a project are described, along with detailed recommendations for implementation. The meeting was jointly organized by NAPC/Nuclear Data Section and NAHU/Dosimetry and Medical Radiation Physics Section.

January 2007

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1. Introduction

Investigations of the use of “heavy-charged particles” (as compared to electrons, photons and neutrons) for radiotherapy were initiated in the early 1970s, with the Bevalac accelerator complex at LBNL in Berkeley playing a pioneer role in the utilization of heavy ions (mostly helium, argon and neon). The rationale for the preferred use of light ($Z \leq 10$) and heavy ions over conventional radiotherapy beams is two fold. First, the energy deposition and dose distribution increases along the penetration depth of the beam, ending with a sharp maximum at the end of the particle range at the point that the very low scattering properties produce a very narrow penumbra in the beam. Second, there is an intense ionisation pattern along the particle path and notably at the end of the range, which results in localized bursts of energy deposition at a microscopic level yielding increased cell killing and thus a radiobiological effect largely superior to that of conventional radiotherapy beams. From the two properties mentioned the physical dose distribution of protons enables accurate dose conformation delivery, and poses a clear advantage over conventional radiotherapy beams; however, the radiobiological effect is only about 8-10% higher than that of photons or electrons. Because of their lower production costs compared to heavy ions, the use of protons in radiotherapy has become well established, and up to date the number of patients treated with this modality is close to forty five thousand.

The radiobiological superiority of ions heavier than protons, with a radiobiological effect of the order of 3-4 times higher than that of conventional beams, has led to an increased interest worldwide resulting in the construction of the Japanese HIMAC clinical facility in Chiba, near Tokyo. HIMAC started the treatment of patients mainly with carbon ions in 1994, and today nearly 3000 patients have been treated in this facility. Whereas heavy ions like the neon beams used in Berkeley have the largest radiobiological effects, these effects also appear in regions close to the beam entrance and in the plateau region, where usually normal tissue is situated. Furthermore and as a consequence of the large penetration of the fragmentation products released by the incident ions, the tail of the dose distribution beyond the Bragg peak may be too high for sparing normal tissue beyond the primary ion range. These two aspects suggest that the ideal ions for radiotherapy are the light ions, and for this reason carbon has dominated the clinical applications at HIMAC. The GSI heavy ion physics research facility in Darmstadt, Germany, has also initiated clinical treatments with carbon ions in 1997, and their results have encouraged the development of facilities exclusively dedicated to proton and carbon radiotherapy. This is an emerging advanced cancer therapy modality, which requires the use of sophisticated computer techniques for patient dose calculation, such as Monte Carlo procedures.

However, the availability of high-quality cross-section data for the simulation of heavy charged-particle interactions is far from being satisfactory. For example, the intra-nuclear cascade models that are employed for cross-section calculations are strictly valid at only high energies (>200 MeV per nucleon), whereas transport simulations must be conducted down to approximately 1 MeV. Data libraries of charged-particle interactions are needed to validate the calculations using nuclear models and for direct use in other type of calculations. There are several available Monte-Carlo particle transport codes with the capability to treat the transport of nucleons, electrons, photons and heavy ions. We expect that most of the existing codes (MCNPX, GEANT4, SHIELD-HIT, FLUKA, etc) will be modified so that they could benefit from the use of updated cross-section libraries.

2. Goals / scope of the meeting

A consultants' meeting was organised to identify the needs for comprehensive evaluated data for nuclear interaction cross sections, including recommendations on types of nuclear data and their accuracy. One further aim was to cover all steps of proton and heavier ion therapy delivery by ensuring discussions between experts in the field of proton and ion therapy, proton and ion dosimetry and proton and ion Monte Carlo simulations.

This meeting was also expected to make recommendations on the need for an IAEA co-ordinated research project, along with the aims and outcomes of such a project.

3. Summary of presentations

Presentation: A. Lomax

The implementation of spot scanning at PSI was presented. Planned treatment covers calculations of spot scanning, flux reduction and the energy deposited as a result of nuclear reactions by means of a simple 1-dimensional model, based on the work of Scheib (1993). For flux reduction, the probability of a nuclear interaction is calculated based on the total cross-sections for oxygen published by Carlson *et al.* (1975), whilst the deposited energy resulting from nuclear interactions is calculated in a simplified 1-dimensional model. 33% of the energy of the lost proton is assumed to be deposited locally (simulating the dose deposited by heavy secondary particles), 33% linearly to the end of the proton range (simulating the dose deposited by secondary protons), and the remaining 33% is assumed to be lost as energy in the form of photons and neutrons which exit the patient. Although rather basic, this model has been found to be robust for predicting measured depth dose curves for a variety of energies and momentum bands (see Pedroni *et al.* 2005). However, it only accounts for effects in the integral dose deposited at any depth, and does not explicitly model the angular distribution of secondary particles. This has been found to be a problem when predicting absolute dose directly from the pencil beam model, particularly for small fields and large air gaps between the nozzle and the patient, where the measured dose could be up to 9% too low compared to predictions from treatment planning. In addition, a 'halo' of dose (presumably secondary protons) has also been directly observed in detailed dosimetric verifications of Intensity Modulated Proton Therapy (IMPT). This effect can manifest itself as a clear under-dosage (as measured) in the peaks, and an accumulation of dose in the 'valleys', particularly for fields where there are sharp peaks and valleys of dose. Again, up to 10% higher dose has been measured in the dose valleys for some IMPT cases.

Due to the above effects, an analytical model for describing the lateral divergence of secondary particles resulting from nuclear reactions has been developed. This model describes the lateral dose 'halo' as a second Gaussian distribution in addition to the primary beam, with the secondary beam width being parameterised on the basis of ionisation chamber measurements at the centre of dose 'frames' of varying sizes (Pedroni *et al.* 2005). In our current implementation, the application of this extended model is applied *post-priori* to all fields after optimisation of the pencil beam weights. By comparing the dose distributions with and without the nuclear interaction effects, it is possible to correct globally the monitor units for the fields such that agreement between predicted and measured doses for all fields is within 1%. However, some problems still remain in the IMPT fields, as the observed effects are local and not global.

Presentation: H. Paganetti

Monte Carlo dose calculations are considered to be the most accurate method to simulate absorbed dose in radiation therapy. Due to the increase in computer power and extensive research on accurate calculation techniques, there is no doubt that Monte Carlo dose calculations will be the dominant method of dose calculation in the near future.

The potential impact of Monte Carlo dose calculation is presumably bigger in proton/ion therapy due to the highly conformal dose distributions and the sharp distal dose gradients when compared to conventional modalities.

The energy region of proton beams is no longer of interest in basic nuclear or particle physics. As a consequence some of the underlying data (e.g. cross sections) are quite old or even incomplete for the energy range and the materials (e.g. human tissues) of interest in proton therapy. Furthermore, today's Monte Carlo codes cover a wide variety of phenomenological or data-driven models to calculate particle tracking. Together with the need for accuracies in the order of 1-2%, this situation constitutes the need for extensive benchmarking of Monte Carlo models to be used for Monte Carlo calculations in radiation therapy.

We have undertaken extensive benchmarking of the nuclear interaction models that can be selected within the GEANT4 Monte Carlo code. Comparisons were made with experimental data (dose distributions and charge distributions in a multi-layer Faraday cup) and with other codes, such as MCNPX. A few examples demonstrate the importance of Monte Carlo simulations (in particular with respect to nuclear interactions) in proton therapy:

- 1) Monte Carlo for treatment technique developments: modelling of the beam delivery system opens various areas where Monte Carlo calculations prove extremely helpful, such as for design and commissioning of a therapy facility as well as for quality assurance verification. Monte Carlo calculations have supported commissioning efforts in understanding the sensitivity of beam characteristics and how these influence the dose delivered.
- 2) Treatment Dose Verification: capability of reading CT data information was implemented into the Monte Carlo code to model patient anatomy. A software link of the Monte Carlo dose engine to the patient database and the commercial planning system was established to allow data exchange. Using a simulation of the ionization chamber reading in the treatment head allows the Monte Carlo dose to be specified in absolute units (Gy per ionization chamber reading). The influence of nuclear interactions on the dose distribution in the patient has been studied.
- 3) Monte Carlo prediction of positron emission tomography: positron emitters such as ^{11}C and ^{15}O are produced via nuclear interactions along the proton beam path penetration and can be indirectly visualized during or shortly after treatment as a spatial marker of radiation dose deposition. Comparison between measured and Monte Carlo simulated PET images can provide feedback on the intended (planned) dose deposition without being impaired by differences between the Monte Carlo.
- 4) Secondary Dose: in radiation therapy, organ dosimetry of the patient is necessary for epidemiological studies of secondary cancer risk, especially for body regions not imaged for treatment planning. Dose distributions and radiation protection quantities such as organ-equivalent and effective doses within the human body are not directly measurable. One of the most versatile and powerful ways of estimating the organ dose distribution in the human body is through the use of computational anthropomorphic

phantoms coupled with Monte Carlo radiation transport algorithms. Cross sections for neutron production have typically large uncertainties.

Presentation: H. Palmans

This presentation was devoted to the importance of non-elastic nuclear data for primary and reference dosimetry of proton beams. The development at NPL of a primary standard for proton dosimetry using a graphite calorimeter requires accurate data for the graphite to water conversion (both for dose conversion and fluence correction). The dissemination of absorbed dose to water for protons and consistency of reference dosimetry in the clinic could be substantially improved by the accurate determination of perturbation factors for ionisation chambers in the proton beam using Monte Carlo simulations and/or experimental verification. Present day best estimates of wall perturbations due to various secondary charged particles (electrons, protons and alphas) are of the order of 0.5% to 1%, but are not applied in clinical dosimetry (cf. the situation in high-energy x-ray beams where perturbation factors of similar magnitude have been applied for 30 years).

NPL has an ongoing calorimetric programme for dosimetry of protons and ions in collaboration with the Clatterbridge Centre of Oncology and other institutes, and is able to contribute to the study of nuclear interaction data with Monte Carlo simulations and attenuation measurements. NPL has considerable experience with GEANT4, MCNPX and PTRAN for the calculation of detector perturbation factors, fluence correction factors and eye therapy beam simulations. The latter demonstrates that several parameters contribute to differences between the results obtained with different codes. Further activities in this field include the study of perturbation factors for various detectors such as alanine, diodes and Faraday cups, as well as the assignment of non-elastic nuclear cross sections to Hounsfield units for the conversion of dose from tissue to water in comparing dose distributions obtained by Monte Carlo simulation and by conventional pencil beam algorithms.

Overall, in order to assure that reference dosimetry does not make a substantial contribution to the overall uncertainty in radiotherapy with protons and heavier ions (typically the uncertainty should be an order of magnitude lower than for clinical dosimetry), considerably more accurate data for total non-elastic and production cross-sections in the therapeutic energy range are required.

Presentation: N. Sobolevsky

Types of nuclear data relevant to the subject of hadron cancer therapy were discussed. Data for both thin (nucleus-target) and thick extended targets are required. Projectiles are light nuclei from proton to neon with energies up to 500 MeV/u, and the target material should correspond to human body tissue. For thin (nuclear) targets, the double differential cross sections of secondary particles/fragments and the production cross sections of PET radioisotopes are of interest. For thick targets, the dose distribution over the target volume, PET isotopes distribution and total and differential yield of secondaries from the target are relevant.

Information about the Landolt-Boernstein Handbook “Production of Radionuclides at Intermediate Energies” (Ed: H. Schopper) by projectiles from protons to α -particles, and about the “Handbook on Secondary Particle Production and Transport by High Energy Heavy Ions” by T. Nakamura and L. Heilbronn (World Scientific, 2006) was presented as examples of compilations of nuclear data relevant to the subject of hadron therapy.

A brief review was given of Monte Carlo hadron transport codes used for the simulation of

interaction of hadron/ion beam with biological tissue in an exclusive manner. These codes in alphabetic order are FLUKA, GEANT4, MCNPX, PHITS and SHIELD-HIT.

A flow diagram of the Russian SHIELD-HIT code was presented, including some details and features such as incorporated nuclear models, the method of stopping power calculation and examples of simulation.

Presentation: O. Jäkel

The pilot project on carbon RT at the German heavy ion lab GSI was briefly presented. An intensity controlled raster scan system is used for beam delivery, which differs significantly from the passive systems used at HIMAC or MGH. This system allows for a variable depth modulation, which has to be accounted for in the modelling of the nuclear fragmentation along with biological effects. The biological model used for the determination of the RBE is called the local effect model (LEM), and uses the radial dose distribution of the particle tracks to calculate the relative biological effectiveness of a mixed ion beam starting from a given X-ray survival curve. Calculated RBE values are the basis for the optimization of the applied dose distributions. The input for the LEM is the underlying particle spectrum at each point in the field, and an empirical description of the radial dose distributions of ion tracks.

The fragmentation model in use at GSI is a one-dimensional empirical transport code (called YIELD), which relies on a parameterisation of geometrical cross sections (Haberer 1994, similar to the Shiver or Tripathi models) for the most important reaction channels. The free parameters are adjusted in such a way that a consistent description of measured fragment yields and depth dose distributions is achieved (Schall 1996, Schardt 1996). While the description at depths up to 15cm in water is very good, at larger depths (around and above 20cm) the agreement with measured depth doses is less impressive. This may be attributed to an underestimation of fragment production or out-scatter of light fragments, which is not included in the model. The MC SHIELD-HIT V2 code gives an overall satisfactory description of the data (Geithner 2006).

The uncertainty in the fragmentation data is acceptable for the calculation of clinical RBE values, and does not seem to be critical. The experimental database for carbon fragmentation cross sections is reasonably good and also includes angular distributions for all fragments (Schardt 1996, Hättner 2006, Matsufuji 2003, Matsufuji 2005, Gunzert-Marx 2004). An emulsion experiment at KEK, Japan, is under way to develop a more complete database (Toshito 2006). This will serve as a benchmark test for a GEANT4 version optimized by KEK scientists for use in RT with C12.

The description of cross sections for the production of PET isotopes is also of great importance in order to analyse the online PET image data acquired for each patient.

Finally, the stopping power data given in ICRU 49 and ICRU 73 are inconsistent with respect to the used I-values.

4. Identification of needs for nuclear data

Order on the basis of sensitivity to nuclear data:

	Protons	Ions
Treatment nozzle simulation and beam characterisation	Total and differential cross sections for materials of beam shaping devices.	Total and differential cross sections for incident ions and secondary charged fragments for materials of beam shaping devices.
Primary standards and reference dosimetry	Total and differential cross sections with high accuracy needed for a limited set of detector materials.	Total and differential cross sections with high accuracy needed for incident ions, secondary charged fragments, and a limited set of detector materials.
Activation for PET	Production cross sections for limited set of tissues.	Production cross sections for incident ions and secondary charged fragments for a limited set of tissues.
Neutron production for protection and shielding	Double differential production cross sections for tissues, beam shaping devices and shielding materials.	Double differential production cross sections for incident ions and secondary charged fragments on tissues, beam shaping devices and shielding materials.
Treatment planning dose calculations	Differential production cross sections for protons and total nonelastic for other charged secondaries.	Differential production cross sections for incident ions and secondary charged fragments.

We need to identify the relative importance of the data for beam shaping devices for all applications.

There is an immediate need for incident carbon beams which covers also all lighter elements (produced in nuclear and fragmentation reactions). There is no immediate need for other incident ions, but such a need may arise in the future. Consequently, data for oxygen ions are not within the scope of this CRP, but may be added to the database at a later stage.

The main materials of interest for reference dosimetry in proton beams are water, graphite and aluminium, as well as maybe a limited list of other materials used in calorimeter and ionisation chamber construction.

Shielding materials are not included in this proposed CRP, but data may be added in the future. Tissue materials for TPS and for activation should be included for implants: titanium, gold, steel.

Maybe differential cross sections are not needed for protons. (cf. Gaussian corrections to lateral dose by TL and EP) – subject to further investigation.

5. Proposed programme

5.1. Selection of data

- Review available data and parameterisations (e.g. Tripathi, Sihver, Shen, Kox, Barashenkov, Tourovsky for protons, etc). A compilation of available data is also required for heavy ions.
- Encourage submission of experimental data for inclusion in EXFOR over the energy region of interest for the application specified above.
- Recommend preferred universal parameterisation for all applications based on the best description of available data.
- Implement selected parameterisations of total and reaction cross sections in different codes by code developers.

5.2. Evaluation of data

Sensitivity analysis for the different applications should be carried out with different codes for representative examples. These analyses could be 3D dose distributions in water, lung and bone for treatment planning, neutron fluence spectra for protection, sensitivity of RBE corrected dose distributions for heavy ion treatment, and graphite to water conversion and perturbation factor of an ionisation chamber for reference dosimetry.

Identify critical gaps in data as a result of sensitivity analysis, and recommend experimental measurements of these data.

Undertake experimental validation of parameterised data for selected applications (e.g. dose distributions in water, multi-layer FC, attenuation measurements, and neutron spectra (bubble detectors and emulsion chamber)).

Investigate the possibility of defining benchmark cases that can be theoretically assessed (cf. Fano theorem for electron transport).

5.3. Monte Carlo implementation

The participants did not make a recommendation concerning the use of specific codes for a given application, neither did they undertake code intercomparison that have the aim of expressing a preference for a particular code.

The work in this programme should be restricted to a limited list of codes with wide-spread use for the applications listed above. The following codes in alphabetical order could be considered: FLUKA, GEANT4, MCNPX and SHIELD-HIT.

Code developers involved in this programme should provide interfaces for different parameterisations and data sets (if not already implemented).

Reference settings relevant to hadronic interactions for each of the Monte Carlo codes should be defined for calculations in this programme and future benchmarking of new code releases. Examples are multiple scattering and straggling options, stopping powers, energy cut-offs and nuclear reaction models.

5.4. Intended outcomes

The following outcomes are expected from the proposed research project:

- Make available experimental and recommended nuclear data parameterisations on the web, recommending new experiments when needed.
- Make available recommended hadronic physics settings for the considered Monte Carlo codes and applications on the web.
- Publication of a technical document (TRS-level).

6. Recommendations from this meeting

- There is a strong requirement for a programme of work focused on nuclear data evaluations for charged-particle therapeutic applications.
- Invite representatives of Monte Carlo code development teams to take part in the programme (one per code).
- Prepare and agree work proposals (early 2007).
- Organise first CRP meeting (late 2007).
- Submit abstracts for ESTRO 2007 (RC), Monte Carlo meeting in Montreal (RC), AAPM 2007 (HaP).

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International Atomic Energy Agency

***Consultants' Meeting on Nuclear Data of Charged-Particle Interactions
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20 – 22 November 2006

Preliminary AGENDA

Monday, 20 November

08:00 - 09:00 Registration (IAEA Registration desk, Gate 1)

9:00 - 10:00 Opening Session

1. Welcoming address – Pedro Andreo, Director – NAPC/Division of Human Health
2. Introduction: IAEA activities on medical applications of nuclear data (R. Capote)
3. Selection of Chairman/Rapporteur

10:30 - 11:15 Administrative and Financial Matters related to participants

Coffee break

11:15 - 13:00 Session 1: Presentations by participants and discussions

13:00 - 14:00 Lunch

14:00 - 18:00 Session 2: Discussion on the Objectives and Program Layout of the CRP

[Coffee break as appropriate]

Tuesday, 21 November

**09:00 - 12:30 Session 2: Discussion on the Objectives and Program Layout of the CRP
(cont.)**

[Coffee break as appropriate]

12:30 - 14:00 Lunch

**14:00 – 17:30 Session 2: Discussion on the Objectives and Program Layout of the CRP
(cont.)**

[Coffee break as appropriate]

19:00 Dinner at Restaurant in downtown Vienna

Wednesday, 22 November

09:00 - 12:30 Concluding Session: Draft Report of the Meeting

[Coffee break as appropriate]

12:30 - 14:00 Lunch

14:00 – 18:00 Concluding Session (cont.)

[Coffee break as appropriate]

Review of the draft including recommendations and suggested actions

Closing of the Meeting

**Consultants Meeting on
“Nuclear Data of Charged-Particle Interactions for Medical Therapy Applications”**

IAEA Headquarters, Vienna, Austria
20 to 22 November 2006

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