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ICTP-IAEA Joint Workshop on Nuclear Data for Science and Technology: Medical Applications

30 September - 4 October, 2013

Introduction to Nuclear Data for Medical Applications

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Opening lecture delivered during the Workshop on Nuclear Data for Science and Technology: Medical Applications, Abdus Salam ICTP, Trieste, Italy, 30 September to 4 October 2013

Topics

- Historical development
- General considerations
- Nuclear data related to medical radionuclides
  - decay data
  - nuclear reaction data
- Nuclear data for radiation therapy
- Motivations for nuclear data measurements
- Interdisciplinary nuclear data activities
  - development of data libraries
  - coordination of international efforts
- Useful literature

Radionuclides for Medical Applications

(Historical Development)

1920s	Biological experiments with natural radioactivity (***Tracer principle***) G. v. Hevesy

Use of Ra/Be-Source

1935	O. Chievitz, G. v. Hevesy *Phosphorus metabolism in rats* (^{32}P)
1938	S. Hertz, A. Roberts, R.D. Evans *Physiology of thyroid* (^{128}I)

Cyclotron Era

1937	J.G. Hamilton, R.S. Stone *Studies with* ^{24}Na
1942	J.G. Hamilton, M.H. Soley *Therapeutic applications of radiophosphorus and radioiodine*
1945	C.A. Tobias, J.H. Lawrence, F. Roughton *Inhalation of* ^{11}CO

Reactor Era

since 1946 Availability of many long-lived radionuclides, e.g. ^{3}H, ^{14}C, ^{32}P, ^{60}Co, $^{125,131}I$ for

- in-vitro studies
- biochemistry, pharmacology, therapy

Renaissance of Cyclotron

since 1960 Production of large number of short-lived radionuclides for in-vivo studies

Several types of cyclotrons have been developed, the smallest one with E_d = 3 MeV to produce ^{15}O and the largest ones delivering protons of several hundred MeV

Today ***Both reactors and cyclotrons are extensively used in production of medical radionuclides***

General Considerations

Criteria for the Choice of a Radionuclide for Medical Application

- **Physical properties**
  - detection efficiency
  - radiation dose

- **Biochemical properties**
  - selectivity
  - suitable kinetics

Factors Contributing to Recent Progress in the Medical Application of Radionuclides

- New efficient automated production methods
- High intensity dedicated accelerators
- Fast labelling, separation and purification methods (GC, HPLC)
- High resolution emission tomographs (SPECT, PET)

Radionuclides for Diagnostic Studies

Requirements

- Short half-life
- Suitable radiation
  (no α or β^- emitter; only EC or β^+ emitter)
- High specific activity

Advantages

- Dynamic studies
- Biological equilibrium undisturbed
- Repeated investigations possible

γ-emitters for SPECT

- E_γ should be 70 – 250 keV
  (overcoming body barrier, high detection efficiency)

Examples: ^{99m}Tc, ^{67}Ga, ^{123}I, ^{201}Tl

β^+-emitters for PET

- Specific detection of 511 keV annihilation radiation in coincidence

Examples: ^{11}C, ^{18}F, ^{124}I

Radiation dose should be minimum

Radionuclides for Therapeutic Studies

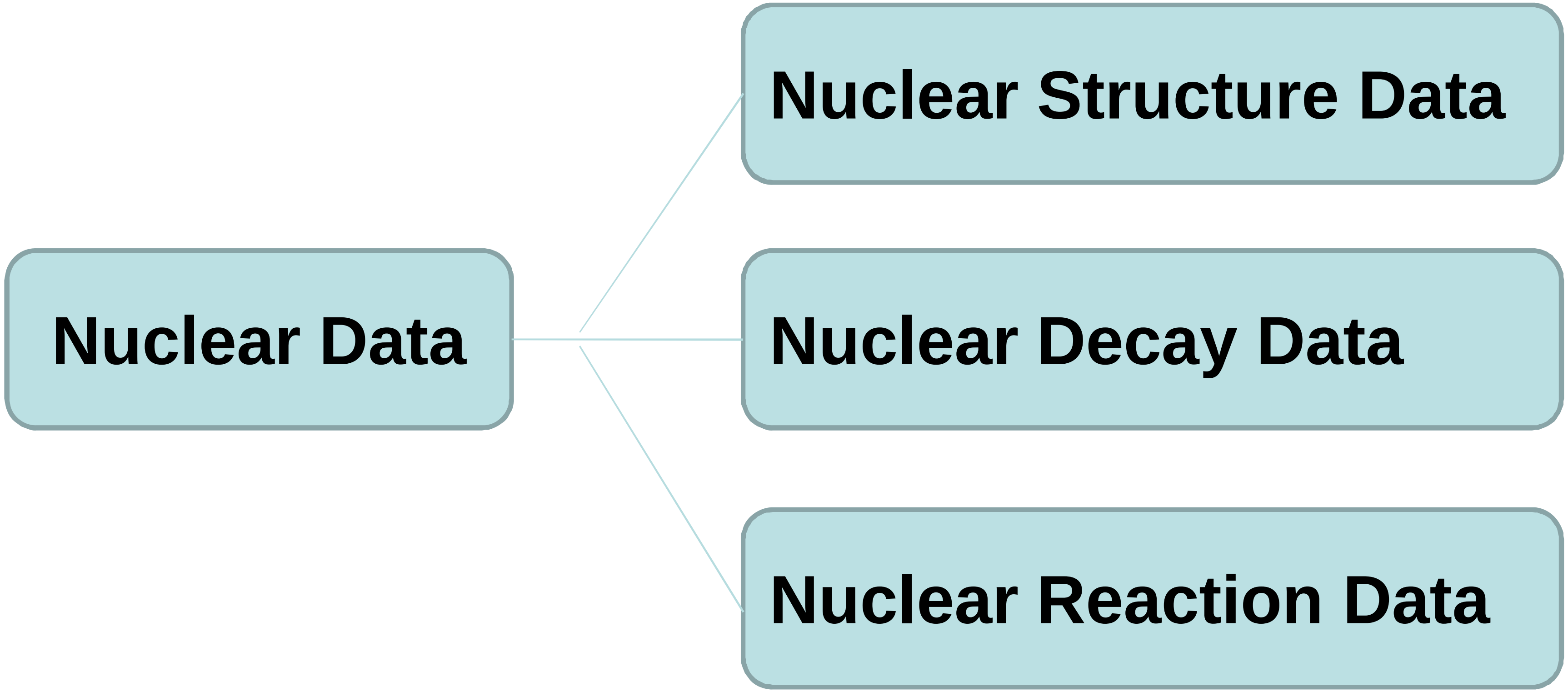
Requirements

- Medium half-life (7 h – 7 d)
- Suitable radiation
  - corpuscular radiation of suitable LET (linear energy transfer) value and range (β^-, e^-, α)
  - low intensity γ-radiation (~ 10 % per decay, $E_\gamma \approx$ 150 keV)
- Chemical reactivity; stability of therapeutical

Radiation dose should be compatible with therapy requirement

Nuclear Data

The term “nuclear data” is very broad; it includes all data which describe the characteristics of nuclei as well as their interactions.

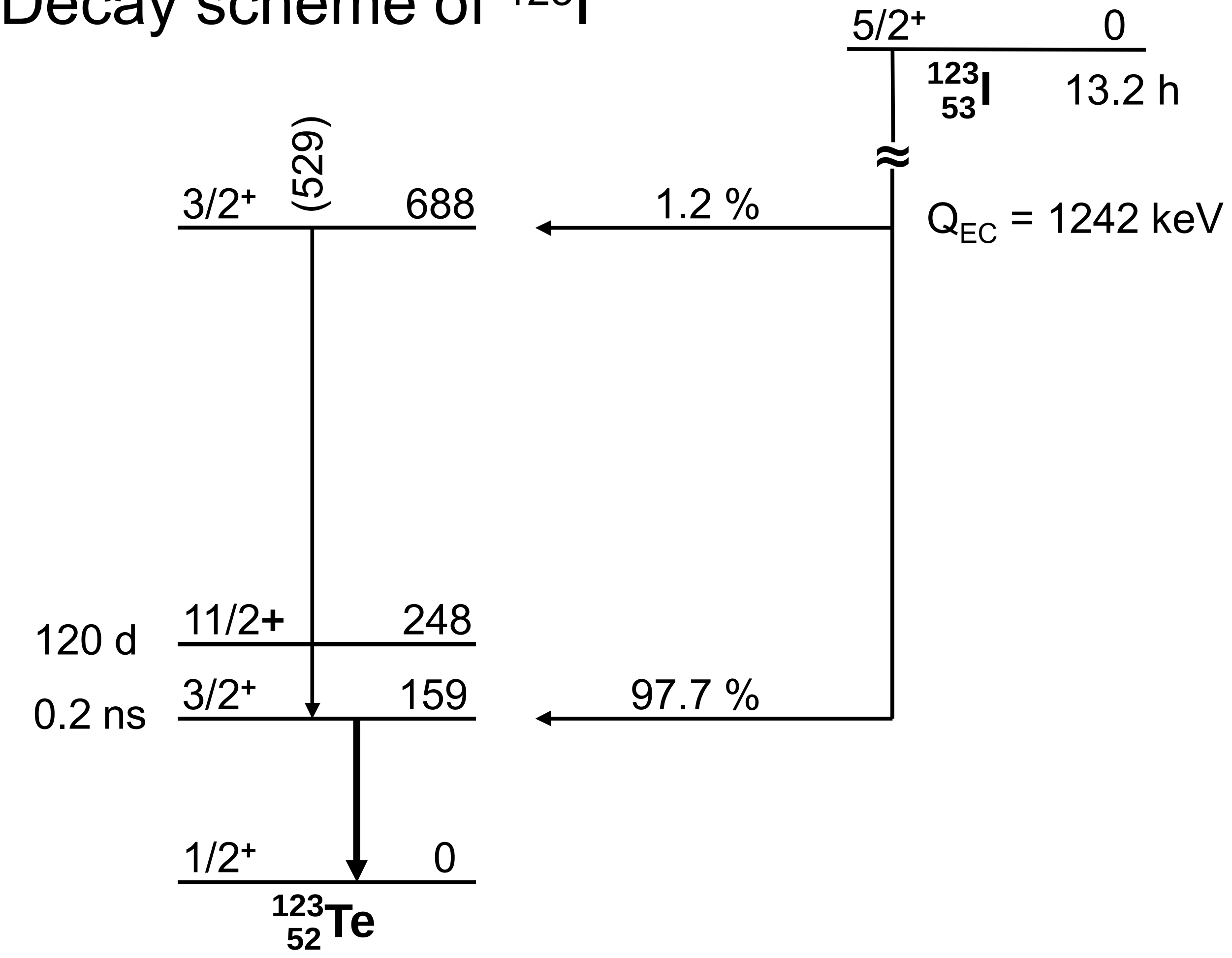


Nuclear Data

- **Nuclear Structure Data**
- **Nuclear Decay Data**
- **Nuclear Reaction Data**

Radioactive Decay Data

Example: Decay scheme of ^{123}I



- Complete knowledge of decay scheme is needed, including information on conversion and Auger electrons

Radioactive Decay Data

Radiation dose calculation

According to Medical Internal Radiation Dose Committee (MIRD), the internal radiation dose ($\bar{D}$) is determined via the expression:

$$\bar{D} = 2.13 \cdot \bar{c} \cdot \sum_{i} n_i \cdot \bar{E}_i \cdot \phi_i$$

where

$\bar{c}$	is the cumulative concentration of activity $\left(Bq \cdot \frac{T_{eff}}{ln2} /kg\right)$
n_i	the number of emitted particles or photons per decay,
E_i	the average energy of the emitted radiation,
Φ_i	the part of the radiation absorbed in the organ,
T_{eff}	the effective half-life of the radioisotope in the organ.

- ***Short-lived single photon and β^+ emitters preferred for diagnostic investigations***
- ***Corpuscular radiation required in endotherapeutic studies***

Nuclear Reaction Data

Neutron data for production in a nuclear reactor

- Production of neutron excess radionuclides

Major reactions: (n,γ); (n,f); (n,p)

$$\text{Generated Activity } A = \frac{m \cdot N_{Av}}{M} \cdot \phi\sigma(1 - e^{-\lambda t})$$

Charged particle data for production at a cyclotron

- Production of neutron deficient radionuclides
- Crucial role of nuclear data in check of impurity

Major reactions: (p,xn); (d,xn); (^{3}He,xn); (α,xn)

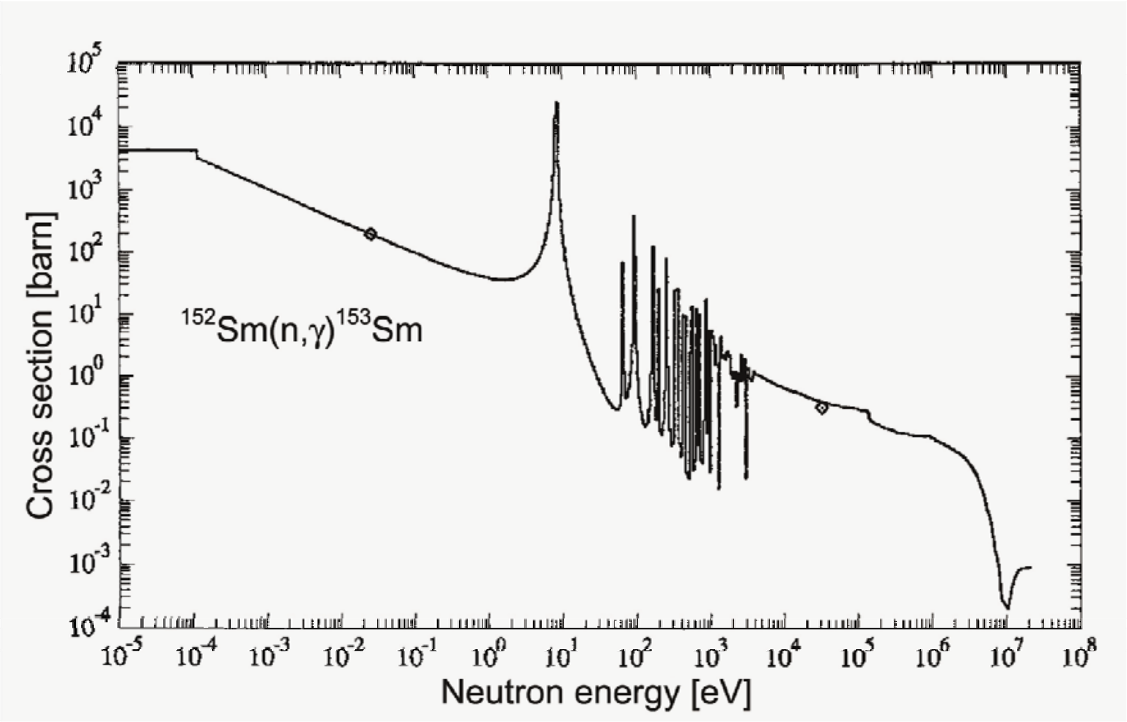
$$\text{Generated Activity } A = \frac{N_{Av}}{M} \cdot I \left(1 - e^{-\lambda t}\right) \cdot \int_{E_2}^{E_1} \frac{\sigma(E)}{(dE/d\rho x)} \cdot dE$$

Nuclear reaction data are needed for optimization of a production route

Radionuclide Production via (n,γ)-Process

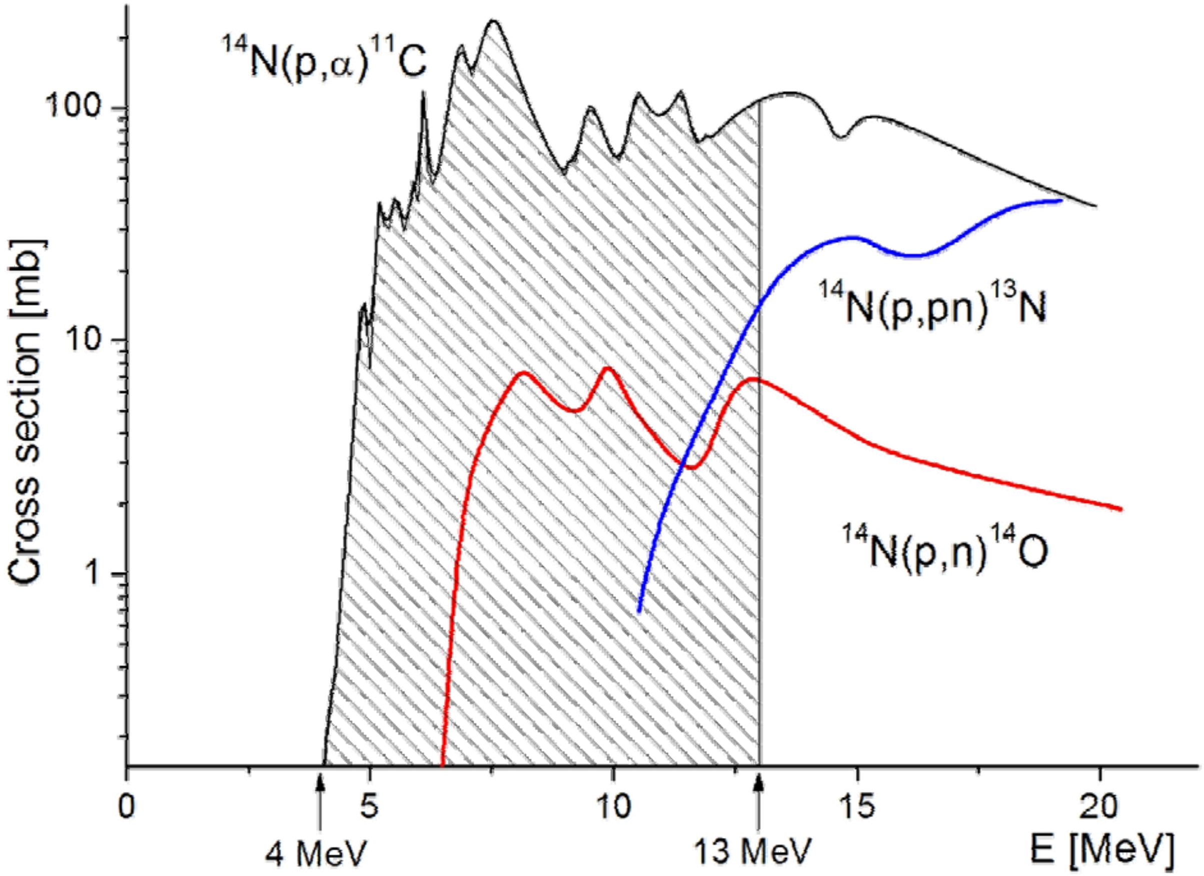
Example:

^{152}Sm(n,γ)^{153}Sm



- Neutron capture in thermal region is most important for production in a nuclear reactor
- ***Double neutron capture possible in high flux reactors, e.g. ^{186}W(n,γ)^{187}W(n,γ)^{188}W***
- Low specific activity overcome via generator systems (e.g. ^{99}Mo → ^{99m}Tc; ^{188}W → ^{188}Re)

Formation of Short-Lived β⁺ Emitters via Protons on Nitrogen



Optimum energy range for ^{11}C production

$E_p = 13 \rightarrow 4$ MeV

Yields at EOB

^{11}C (20 min)	80%
^{13}N (10 min)	~ 5%
^{14}O (70 s)	~ 20%

Kovács et al., RCA **91**, 185 (2003).

Radiation Therapy

- Biological changes under the impact of radiation
- Of significance is linear energy transfer (LET) to tissue

Types of Therapy

- ***Photon therapy***: use of ^{60}Co or linear accelerator (*low-LET radiation*)
- ***Fast neutron therapy***: accelerator with E_p or E_d above 50 MeV (*high-LET radiation*)
- ***Proton beam therapy***: accelerators with E_p = 70 -250 MeV (*treatment of deep-lying, rather resistant tumours*)
- ***Heavy-ion beam therapy*** (*rather specialized; limited application*)
- ***Boron neutron capture therapy*** (BNCT): use of low energy neutrons (still at development stage; *pharmacological problem)*

Radiation Therapy

(Cont´d)

Atomic and nuclear data required to

- calculate radiation transport
- calculate the absorbed dose at a point in the tissue
- optimise the design of the treatment delivery system

Data Needs (up to 250 MeV)

- Total and non-elastic cross sections
- Production yields and average energies of emitted n, p, d, α, γ
- Double differential cross sections at various incident energies
- Excitation functions for the formation of radioactive products

Atomic data are of more significance than nuclear data

Nuclear Data Measurements

Motivations

Reaction data

- Search for alternative route of production of an established radionuclide
  - jeopardy in supply
  - demand for higher purity
- Development of novel radionuclides for medical applications

Decay data

- Removal of discrepancies and uncertainties, e.g. in
  - β^+ branching in ^{120}I, ^{124}I, ^{76}Br, etc.
  - intensities of γ-rays
  - end point energies of β^- and β^+ emitters
  - intensities of low energy conversion and Auger electrons

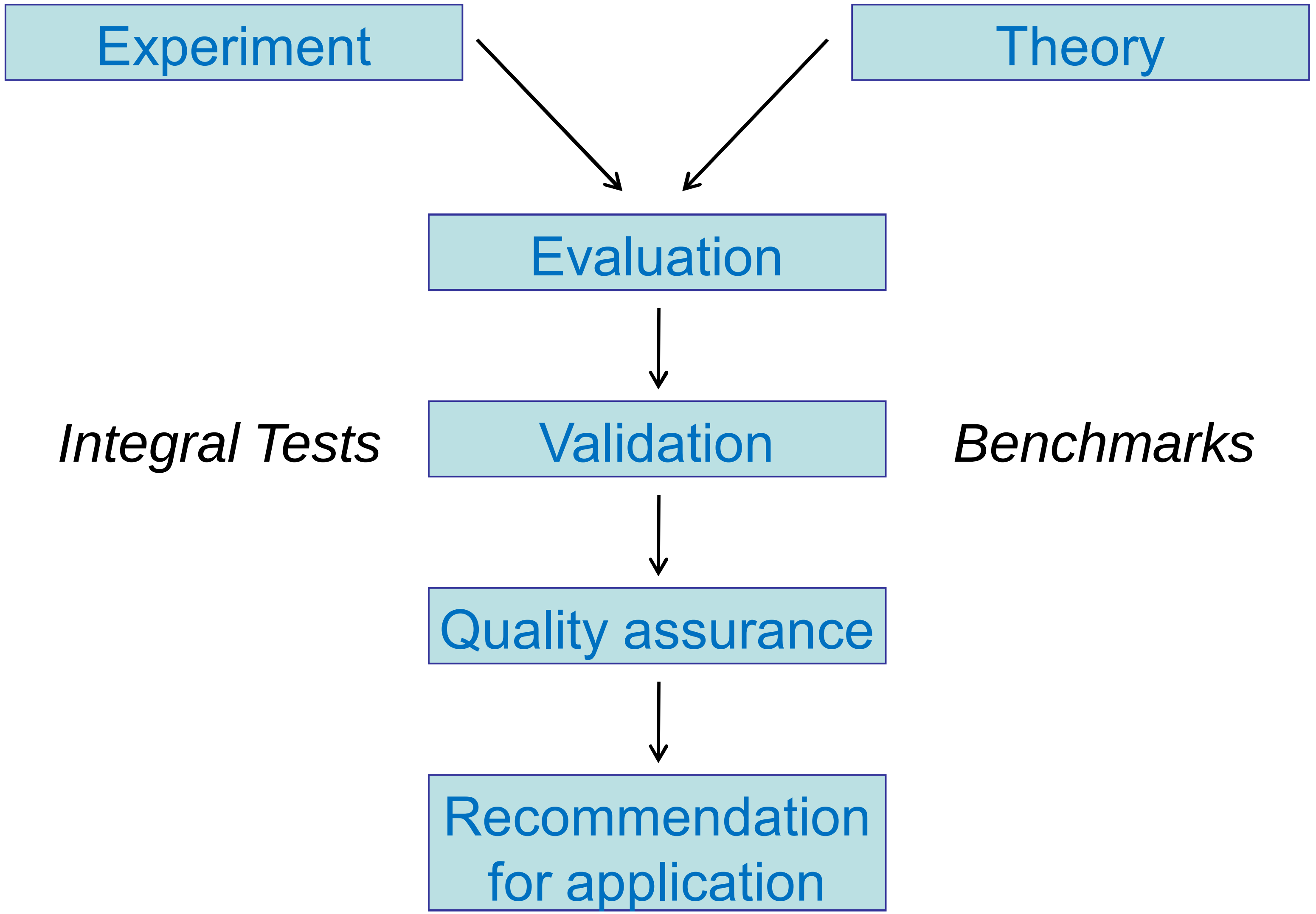
Interdisciplinary Nuclear Data Activities

- **Experimental measurements**
  - on-line and off-line methods
  - interdisciplinary techniques
  - detailed description of experiment, uncertainties and their correlations

- **Compilation and standardization**
  - collection of data in a uniform format (EXFOR)
  - standardization of data (development of a reliable data file)

- **Nuclear theory**
  - improvement of known models and parameters
  - development of new models of high predictive values

Nuclear Data Development for Applications



Experiment

Theory

Evaluation

Integral Tests

Validation

Benchmarks

Quality assurance

Recommendation for application

Nuclear Data Centres

- NNDC, Brookhaven, USA
- OECD-NEA Data Bank, Paris, France
- IAEA Nuclear Data Section, Vienna, Austria
- Nuclear Data Centre, Obninsk, Russia

International Co-ordinating Bodies

IAEA
(INDC)

- Energy related applications
- Non-energy related applications

Functions

- EXFOR
- Coordinated Research Projects
- Special Data Files
- Training (together with ICTP)

NEA
(NSC)

- Energy related applications
- Spin-off effects of nuclear energy
- Nuclear sciences

Functions

- JEFF
- Data Bank
- Conferences

Observations Regarding Nuclear Data for Medical Applications

- ***Radioactive decay data***

generally well characterised and well documented; some deficiencies
(Table of Isotopes; Decay Data Sheets; Nuklidkarte; MRID Compilation)

- **Nuclear reaction data**

mostly available in the context of energy research
Much less effort has been devoted to medically oriented data.

Radionuclide production: High accuracy data needs (uncertainty ≤ 10 %)

Radiation therapy : Extensive data needs, though not with high accuracy (uncertainty ≤ 25 %)

Several coordinated efforts are underway,
mostly under the auspices of IAEA

Useful Literature

Monographs

1. S.M. Qaim (Editor)
   Nuclear Data for Medical Applications
   Special issue of Radiochimica Acta **89** (2001), pages 189-355

2. IAEA-CRP on „Charged Particle Cross Section Database for Medical Radioisotope Production: Diagnostic Radioisotopes and Monitor Reactions“, IAEA-TECDOC-**1211** (2001), pages 1-285

3. S.M. Qaim, F. Tárkányi, R. Capote (Editors): IAEA-CRP on „Nuclear Data for the Production of Therapeutic Radionuclides“, IAEA-Technical Reports Series No. **473** (2011), pages 1-377

4. K.F. Eckerman, A. End (Editors): MIRD: Radionuclide Data and Decay Schemes, 2nd Edition, Society of Nuclear Medicine, Reston, VA, USA (2011), pages 1-671

Reviews

5. S.M. Qaim
   Decay data and production yields of some non-standard positron emitters used in PET
   Quarterly J. Nucl. Med. **52** (2008), pages 111-120

6. S.M. Qaim
   Development of novel positron emitters for medical applications nuclear and radiochemical aspects
   Radiochimica Acta **99** (2011), pages 611-625

7. S.M. Qaim
   The present and future of medical radionuclide production
   Radiochimica Acta **100** (2012), pages 635-651

8. A.L. Nichols
   Radioactive decay data: powerful aids in medical diagnosis and therapy, analytical sciences and other applications
   Radiochimica Acta 100 (2012), pages 615-634