Nuclear excitation functions for medical isotope production: Targeted radionuclide therapy via natIr(d,2n)^{193m}Pt

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Contents

Chapter 1

Targeted radionuclide therapy

All written in this chapter needs to be rewritten as a lot of the text is just copied from various citations.

Today, multiple options for treatment of cancerous tissue are available, such as chemotherapy, surgery, immunotherapy, external beam therapy, bracytherapy and targeted radionuclide therapy. The latter three are treatment types utilizing ionizing particles to induce damage to the DNA. In external beam therapy X-rays, high-energetic gamma-rays, or accelerated particles like protons and heavier ions are focused externally towards the tumor, and for brachytherapy, and in bracytherapy an unsealed radioactive source (usually a wire or pellet containing for instance a $^{-}$-emitter), is placed in proximity to tumor (handbook of nuclear chemistry, p. 2180). Targeted radionuclide therapy is an emerging alternative, which can deliver a cytotoxic level of dose to the cite of disease (handbook of nuclear chemistry p. 2180). It offers a patient-specific treatment dependent on choice of radiopharmaceutical which targets a type of tumor or cell. A radiopharmaceutical consists of a radionuclide and a cell-targeting molecule called a tracer. Meanwhile brachytherapy and targeted radionuclide therapy are limited by the cancer location and the existence of metastasis, along with required knownledge of the tumor to maximise the dose over the tumor and minimizing the dose to healthy tissue (Handbook of nuclear chemistry, p. 2180), targeted radionuclide therapy utilizes radiopharmaceuticals which are typically injected intravenously and utilized the biochemical pathways in the body. thus with an appropriate tracer, targeted tissue with an high uptake of the radiopharmaceutical will receive a high dose, and healthy tissue can be spared (Yeong2014).

A therapautic agent need to have the two components optimized for the radiation from the radionuclide to have a high probability of being deposited in the tumor, and ideally cytotoxic dose to all cancerous cells within a tumor and sparnig all healthy cells. The decay mode and radiation range are in coherence with the size and location, as well as the geometry of the tumor, and ranges from multicellular, cellular and subcellular ranges are typically accomplished with beta, alpha and auger electrons, respectively. However, geometrical factors of both the distribution and the tumor it self can have a degree of variations in the dose distribution due to differences in cross fire dose and the fraction of the radiation bound to the cell that is deposited in the tumor. Particularly apparent for micrometastatic disease which presents as small cluster of tumor cells, magingying the impact of these factor. In addition, it is important to achiece a homogeneous dose deposition within the tumor, so that regrowth from an untreated subpopulation will be avoided. For the radionuclide, along with range and decay mode, the half-life production method, chemistry and biological behavior are important characteristics (handbook p. 2180-2182). For the tracer, a rapid blood clearance and transport (6, p. 145) and high uptake and retention in the tumor (9. p. 2) (special curriculum p. 4) are important characteristics. It can target the desired cells by for instance a specific receptor, enzyme, membrane, transporters or antigens (6, p. 145). Radiometals are also used, which consists of a bifunctional chelator, which is a molecule containing molecules which can donate a lone pair of electrons, like nitrogen, oxygen or sulfur. If the radiometal has an oxidation state of 3^{+}, it will be tighlty bound by the chelator, and can transported to the tumor (special curriculum p. 4-5).

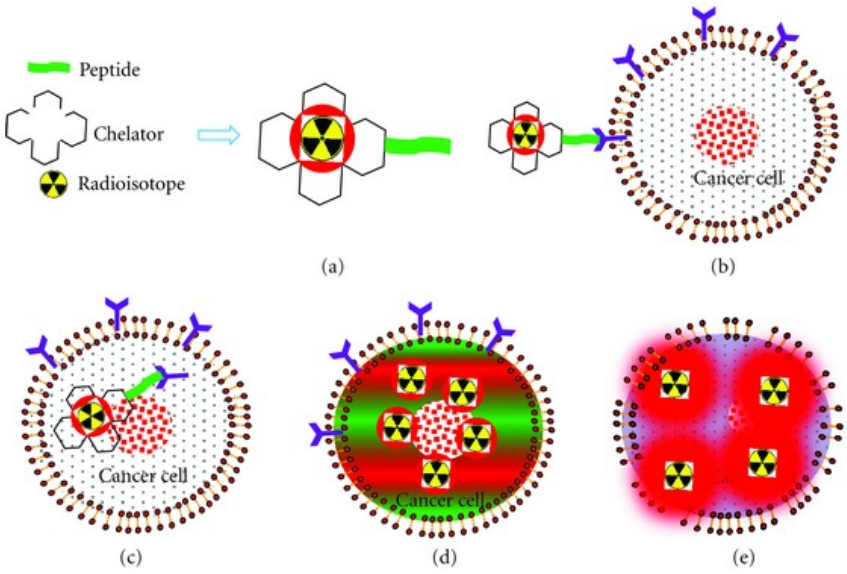

Figure 1.1: A radionuclide is bound to a chelating agent, and with a peptide, the radiopharmaceutical targets the cancer cells. Figure is from citation [8] in the special curriculum.

Figure 1.1 shows an illustration of how a radionuclide is attached to a chelator, and is transported to cancer cells with a specific peptide.
Whenever something is cited like (3), it means citation 3 in special curriculum Special curriculum p. 4: as mentioned above there are many requirements before a radiopharmaceutical can be used clinically, there are physical properties concerning the radionuclide, such as physical half-life, decay-mode and decay product, radiation energy and in-tissue range, and biological properties concerning the tracer such as tissue targeting, biological half-life, retention in tumor and the uptake in healthy tissue (3). Thus, the radiopharmaceutical requires two components in which complement each other to deposit the dose in the cancerous tissue.

In nuclear medicine, the effective half-life of the radiopharmaceutical is important as it takes both the physical half-life and the time it takes for the radiopharmaceutical to be cleared or excreted from the body (3). Thus it should be long enough to permit radiosynthesis and qauality control. SHould be compatible with the pharmacokinetics of localization in tumor and clearance from normal tissue. However, as for therapy, high radiation dose is desired, which is easier to achieve with shorter half life, so that should also be compensated for. The choice of radionuclide should match the uptake rate and the retention, to avoid radioactive waste handling and dose to healthy tissue (3). Therapautic radionucldies typically have half-lives in order of a few hours to several days (9, p. 1) (special curriculum p. 4).

Knowledge about the decay products are also important, if unstable, how it the dose distributed, and how long range, half life, blabla, and if unstable, is the daughter contributing to a cytotoxic effect, or taking part of the natural stuff in the body.

In addition, the chemical-biological properties are important, as it must be chemically possible to attach radionuclide to the targeting molecule. Also, the bond must be stable in the body, over a time period which is stable as long as the physical half life. (handbook p. 2185)

1.1 Particle interaction in tissue

Ionizing radiation are particles with sufficient energy to cause ionizations along the particle track, thus separating an atom and one or more electrons. The free electron(s) can ionize further, and the positive ion can cause undesired reactions. DNA is a large molecule with two strands bound in a double helix structure. Each strand is composed of sugar and phosphate groups, and nitrogenous bases which bind

the two strands (book p. 11). These bases are called adenine & guanine amd cytosine & thyamine (always bound pairwise), and are bound through weak hydrogen bonds which are exposed for strand breaks. The cell is equipped with an impressive repair mechanism, and unless both strands of the DNA is damaged, called a double stranded break (DSB), most damages are repaired. Radiation damages in the DNA can be caused directly by the ionizing particle or indirectly via free radicals, which are subject to other ionizations. Since the body contains large amounts of water, ionization of water molecules giving for instance $H^{\bullet}$ or $OH^{\bullet}$ are important damaging factors. Damages induced in the DNA can be lethal to the cell and either cause apoptosis or mutation in which can cause cancer. In therapy, the goal is to make malignant cells to undergo apoptosis, thus DNA is referred to as the target (book, p. 9). Choosing a particle with a high probability of inducing damage will induce multiple double stranded breaks if passing near by (special curriculum).

Linear energy transfer (LET) describes the energy absorbed by the medium, and is defined as the average energy (typically in keV) deposited per unit length (typically measured in μm) of the density material (book, p. 101)

$$\text{LET} = \frac{dE}{dx} \tag{1.1}$$

To maximise the chances of inducing damages in the DNA and minimizing exposure of healthy tissue, choosing a particle with a high linear energy transfer is important in targeted radionuclide therapy. Figure 1.1 illustrates how β^{-}-particles, alpha-particles and auger electrons deposit energy on the scale of DNA.

A medium consists of positively charged nuclei and negatively charged electrons. Charged particles have a short range in a medium compared to neutral particles, as the Coulomb force forces the particle to interact continuously along the path either by scattering inelastic with the atomic electrons or scattering elastic with the nuclei. Elastic scattering is the less dominant process, where the energy loss is small, as long as the nuclei in the medium are larger than the incoming particle(Techniques for Nuclear and Particle Physics Experiments, William R. Leo, p. 21). Inelastic collisions dominates where the atomic electrons are either excited or ionized (which citation???? Instrumentation book?). Under the assumption that the collision is elastic, the collision is head-on and the particle has high energy, the maximum energy transfer can be calculated using conservation of momentum and energy

$$Q_{\max} = \frac{4m_e M}{m + M} E \tag{1.2}$$

where m_e is the mass of an atomic electron, M is the mass of the incoming charged particle and E is the kinetic energy of the incoming charged particle[1]. While LET describes the energy transferred per unit length, the stopping power describes the energy loss of a charged particle per unit distance. The collision loss for heavy charged particles (protons and above) at high energies is therefor low. The stopping power for heavy charged particles (protons and up) is described by Bethe-Block. As the particle slows down, the more energy per unit length will be deposited, as the charged particle picks up electrons. This is known as the Bragg peak. most of the energy is deposited near the end stop. The stopping power of heavy charged particles are proportional to the charge of particle and the inverse velocity squared. Therefor, particles with a higher charge will have a higher Bragg-peak and a shorter range in tissue, if energy was the same. This behaviour of heavy charged particles is especially useful in external beam therapy and is utilized to have a very specific dose over tumor as the dose before is low and the dose after bragg peak is zero (instrumentation, p. 27-28).

Electrons can experience energy loss either from collisions, or via the electromagnetic radiation that arises when electrons are loosing energy (bremsstrahlung), due to the small mass. However, for energies up to a few MeV, the collision energy loss dominates (Techniques for Nuclear and Particle Physics Experiments, WilliamR. Leo, p. 37). For electrons, the maximum energy transfer per collision is half of the initial energy, which means that electrons lose energy fast via collisions. Electrons

[1] https://ocw.mit.edu/courses/nuclear-engineering/22-55j-principles-of-radiation-interactions-fall-2004/lecture-notes/energydeposhcp.pdf

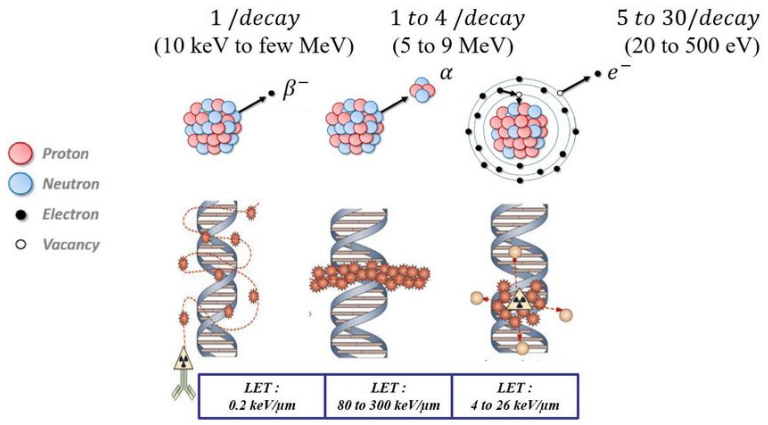

Figure 1.2: The figure illustrates how β^--particles, α-particles and auger electrons deposit their energy on the scale of DNA.

scatters rapidly, and changes direction continuously due to the equal mass of the atomic electrons. The collision stopping power is a modification from Bethe-Block, such as changing $W_{\max} = T_e/2$. The energy loss of electrons fluctuates much more than heavy charged particles which is due to much greater energy transfer per collision and to the emission of bremsstrahlung. To absorb major part of the electron's energy, is a few collisions, and results in greater range straggling. (instrumentation p. 42)

Beta-electrons have a continous spectrum of energies and absorption of beta decay electrons exhibit behavour which is well approximated to an exponential form (instrumentation p. 42). Low energetic electrons are small in mass to large angle deflection by scattering from nuclei (p. 48).

Photons and neutrons however are neutral particles and are not energy-degraded. Instead neutral particles are attenuated as a function of distance traversed x and the attenuation coefficient μ of the material

$$I = I_0 e^{-\mu x} \tag{1.3}$$

where I is the intensity as a function of distance and I_0 is the intensity at x=0. X-rays produced from a X-ray tube and gamma-rays degrades exponentially, thus have a high dose over a long distance. As gamma emitters are not directly used in targeted radionuclide therapy, the gammaradiation following alpha or beta decay, or X-rays following electron capture or internal conversion needs ti be taken into account.
For high energetic X-rays, there is also a build up effect, where the photons induce ionizations, and the free electrons contribute to a higher dose. This is utilized in external beam therapy, maximizing the dose over the tumor.

Figure 1.3 illustrates how various particles interact in a medium. For photons, there is an exponential tale, and for high energetic X-rays it is clear that there is a build up effect. For protons, the Bragg peak is very evident. For 22 MeV electrons, it is clear that there is bremsstrahlung energy loss due to the exponential tale.

Figure 1.4 shows an overview of the ranges of auger electrons, 5.3 MeV alpha particles, low and high energetic β^- particles of 0.15 MeV and 1.7 MeV. Thus β^--particles have a relatively long range in tissue, and can be up to a few mm dependent on the energy spectrum (handbook, chapter TRNT (TARGETED RADIONUCLIDE THERAPY). Beta-particles have relatively low LET and are thus suited for treating large tumors, but the dose to healthy tissue is hard to avoid. Alpha-particles have

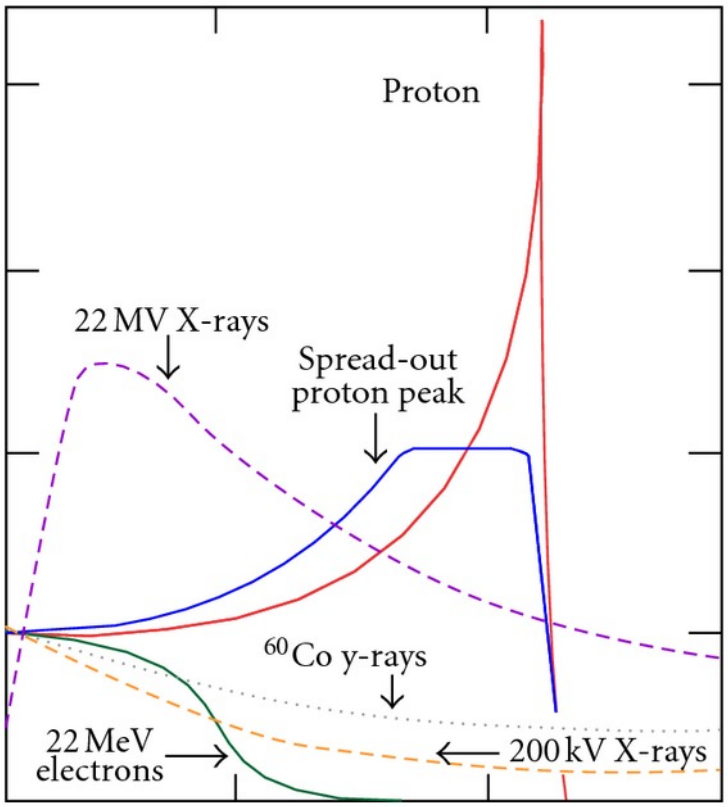

Figure 1.3: Medium depth along x-axis, energy deposition in tissue (or dose?) on y-axis. Find citation in special curriculum.

short range in tissue, typically a one to a few cells in diameter. Has a high LET-value, radiation with LET=100 keV/μm has the distance between ionizing events is nearly identical to that between DNA strands increasing the probability of creating highly cytotoxic double strand breaks (handbook, TRNT). For low energetic electron emitters such as auger emitters, the range is so low that in order to deposit energy in the DNA, must be incorporated into the cellular nucleus. Thus, it will only affect the cell targeted, and as we can see in figure 1.1 when incorporated into DNA, will induce many breaks and kill cell!! (book: chapter targeted radionuclide therapy, whole paragraph)

1.2 Production of radionuclides

The radionuclide availability is an important factor, and must obviously be high. Reactors, cyclotrons and natural decay chains have traditionally been used as radionuclide sources (Handbook of ... , p. 2185). Proton rich nuclei are typically produced in accelerators/cyclotrons using positively charged particles, and neutron rich nuclei are typically been products of fission or produced in the neutron flux resulting from fission in a reactor. Thus therapautic radionuclides producing β^--emitters needs neutrons, which are the main source of reactors. With research reactors today agin ([3], in special curriculum p. 10), alternative production routes to produce critical medical radionuclides.

There are many different production routes available for a single radionuclide, dependent on choice of target, particle beam and beam energy. The production route has an associated reaction cross section which is dependent on the beam energy. The nuclear cross section data is very important in optimization of production processes, achieving the maximum yield of the desired radionuclide combined with the minimum level of radionuclidic impurities ([9], in special curriculum p. 3). A high degree of radionuclidic purity is required for therapautic radiopharmaceuticals depending on the

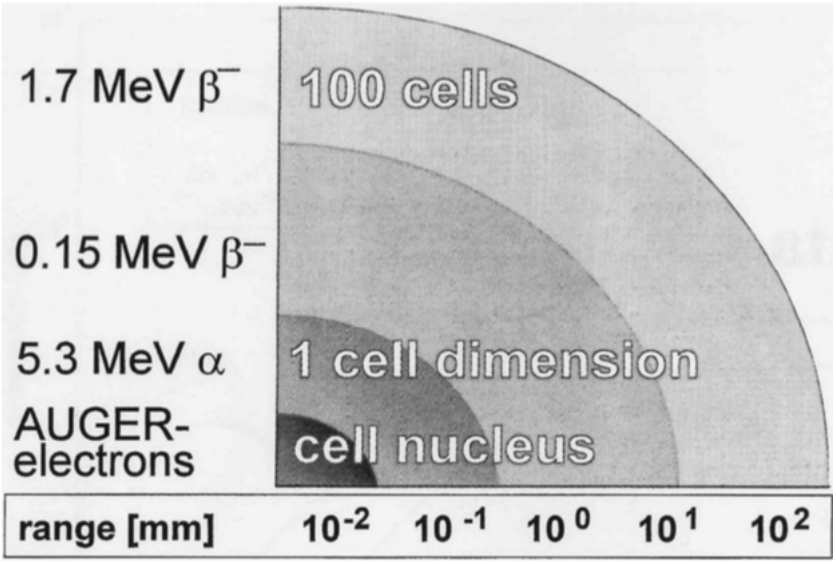

Figure 1.4: The figure illustrates the ranges of auger electrons, 5.3 MeV alpha particles and low and high energetic β^- particles.

nature of the molecule that will be labelled, specific activity (GBq/mmol) may also be important consideration. It is impossible to chemically separate isotopes of the same element ([4], in special curriculum p. 10). We want to be sure that the what is injected into the patient does not have isotopic impurities which gives undesired dose to the tissue, nor will we have isotopes with no therapautic effect, both for most effective treatment, but especially in cases where the body does not excrete the element from the body, and we can have poissoning. Carrier-free production which are molecules which exclusively contain the desired radionuclides is desired because it gives the highest specific activity. The only option to minimize impurities is to choose an appropriate energy windown which minimizes the production of co-products.

There already exists large amounts of information on neutron induced reactions. However the information on charged particle induced reactions is not as strong so we need more data on this behalf ([4] in special curriculum p. 10). Production of medical radionuclides should be cheap and available for everyday medical purposes. Cyclotrons good: Accelerators can be small in size and handled easily by medical personnel. Many hospitals which performs nuclear medicine even hve a cyclotron facility on site, which is advantageous as its practical to avoid travelling logistcs and to have medical radionuclide supply in proximity og examination/treatment site.

1.3 ^{193m}Pt as a potential therapautic agent

^{193m}Pt ($t_{1/2}$=4.33 days) is an auger-emitting isomer which decays by isomeric transition (100%) to the long-lived ^{193g}Pt groundstate ($t_{1/2}$=50 years). Radionuclides produced from deuterons on natural iridium such as ^{191}Pt, ^{193m}Pt, ^{192}Ir and ^{194}Ir are believed to have potential in medicine, like chemotherapy, brachytherapy, radioimmunotherapy and imaging (Tarkanyi et.al 2006). Platinum radionuclides are of special interest, as platinum is the main element in chemotherapautic agents such as cisplatin, which is a drug which is used clinically in treatment of testicular and ovarian cancer mainly, but also to treat esophagus, head and neck and bladder cancer[5]. Cisplatin (cis-dichlorodiammine platinum(II)) is an inorganic molecule which contains one stable platinum atom surrounded by two clorine atoms and two ammonia molecules (NH_3). The cisplatin-molecule enters the cell nucleus, and binds to the DNA, example-wise shown in figure 1.5, where the clorine-atoms are de-attached and the platinum-atom binds through covalent bonds to the DNA base guanine (and in some cases adenine, is that correct?), and breaks the bonds between the DNA nitrogeneous bases.

[5]https://www.sciencedirect.com/science/article/pii/S0969804399000822?casa$_token$ = $ZLJ8YPQzGZMAAAAA$: $264QzKWpH8Kv6iHotiGMeoHTk8jKqmnoDgf709SrAD8BUWVwbRXriZbHgkYO_tHg - 2qyX3Hvt9E$

Cisplatin thus targets the DNA. One of the major challenges with cisplatin is the chemical toxicity, but when auger-emitters such as ^{193m}Pt or ^{195m}Pt replace the stable platinum atom, the local auger-damage effect increases the chemical damage of cisplatin, suggesting that a smaller amount of the drug is required, and chemical toxicity can be avoided [6].

By replacing either of the stable nitrogen atoms with the PET-radionuclide ^{13}N ($t_{1/2}$=9.965 minutes), or by a radionuclide platinum, where ^{191}Pt ($t_{1/2}$=2.83 days, decay by electron capture (100%) to ^{191}Ir (stable)) , ^{193m}Pt and ^{195m}Pt ($t_{1/2}$=4.010 days, decay by isomer transition (100%) to ^{195g}Pt (stable)) is of special interest, cisplatin can be used for imaging or therapy[7], but therapy is most common.

As ^{191}Pt is electron-capture emitter, can be used in imaging, with for instance 129.4 keV (38.0%) or 172.19 keV (43.2%). Combining ^{191}Pt with a therapautic agent might be possible for theranostic pair with either ^{193m}Pt or ^{195m}Pt? Can be combined with therapy as it releases auger electrons?

Decay mode: For ^{193}Pt, there are three states, the isomer state at 149.8 keV, with nuclear spin $13/2^+$ (4.33 d), a state at 14.3 keV with nuclear spin $5/2^-$ (2.52 ns), a state at 1.6 keV with nuclear spin $3/2^-$ (9.7 ns) and the ground state at 0.0 keV with nuclear spin $1/2^-$ (50 y)https://www.nndc.bnl.gov/nudat2/getdecays V.S. Nuclear data sheets for A=193. Nucl. Data Sheets. 32, 593-679, 1981. here write about gamma-decay and that the probability for M6 or whatever transition is improbable. The populated isomer states decays from 149.8 keV to 14.3 keV releasing a 135.50 keV photon (0.1145475%), from 14.3 keV to 1.6 keV releasing a 12.634 keV photon (0.70%), and from 1.6 keV to the ground state releasing a 1.642 keV photon (0.0321). The photon abundance is thus low, and this isomer is not well suited for imaging. Due to the low intensity of the gamma-rays, it might be difficult to detect. There are X-rays too, but they overlap with other nuclei. Since the gamma-rays are weak, the IC probabilities are 99.89%, 99.33% and 99.99% for each state respectively, calculated by subtracting 100 - gamma-intensity [8]. This also indicates that the phondon abundance is very low, as well high very high prob of low E electrons :D

In all decays, there are certain quantities in which needs to be conserved; angular momentum (ℓ) and parity (maybe ℓ should be written as L instead??). Krane says that a multipole of order ℓ transfers angular momentum $\ell\hbar$ per photon (Krane, p. 333). A nuclear state has a definite angular momentum (angular momentum and spin) and parity, and if a gamma-transition is to happen between two states, the photon must connect the two states by conserving angular momentum and parity. In order for the quantity ℓ to be conserved, the angular momentum can be integer values between

$$|I_i - I_f| \leq \ell \leq I_i + I_f \tag{1.4}$$

For the decay of ^{193m}Pt (E level=149.8 keV) to the excited state (E level=14.3 keV), the spin and parity change is from $13/2^+$ to $5/2^-$, so $\ell = 4, 5, 6, 7, 8, 9$. The parity decides the wether the radiation is electric multipole or magnetic multipole (equations from Krane p. 331),

$$\pi(ML) = (-1)^{\ell+1}, \quad \pi(EL) = (-1)^{\ell} \tag{1.5}$$

The electric decays have even parity when ℓ=even, and magnetic has even when ℓ is odd. If parity is unchanged in the reaction ($\Delta\pi$ =no), the electric multipoles are even and magnetic multipoles are odd. If the parity does change ($\Delta\pi$ =yes), there would be odd electric and even magnetic multipoles. Hence the possible transition from $13/2^+$ to $5/2^-$ are whenever $\Delta\pi$ =yes and $\ell = 4, 5, 6, 7, 8, 9$, which gives possible M4, E5, M6, E7, M8 or E9.

In general, the lowest possible multipole dominates, and the emisssion of multipole of one order higher (L+1 than L), is reduced by a factor ca 10^{-5} (Krane p. 335, important!!). Thus, a multipole of order 4 or 5 has a low probability of occuring and thus the isomer has a long half life. In comparison to decay from isomer state, decay from $5/2^-$ to $3/2^-$ gives possible radiation, $\ell = 1, 2, 3, 4$, with no

[6] http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.987.2577rep=rep1type=pdfpage=506, p. 493

[7] https://www.sciencedirect.com/science/article/pii/S0969804399000822?casa$_t$oken = $ZLJ8YPQzGZMAAAAA$: $264QzKWpH8Kv6iHotiGMeoHTk8jKqmnoDgf709SrAD8BUWVwbRXriZbHgkYO_tHg - 2qyX3Hvt9E$

[8] http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.987.2577rep=rep1type=pdfpage=506, p. 496

parity change, and $\Delta\pi$ =no, gives possible M1, E2, M3, E4, and from $3/2^-$ to $1/2^-$ gives $\ell = 1, 2, 3, 4$, which also gives M1,E2, M3, E4.

Half life: the decay rate constant is the sum of the decay rates of all the populates states transitions, $\lambda = \lambda_{13/2^+} + \lambda_{5/2^-} + ...$

1.3.1 Gamma-decay and isomeric transition

Gamma-decay is the lowering of the excitation energy by the release of a photon, with an energy ΔE equal to the energydifference in the two states. The typical half lives of gamma-emission are less than 10^{-9} seconds, however, longer lived states of a nucleus which is not the ground state is called an isomer, and the gamma-decay of an isomer state is called isomeric transition (Krane, p. 175). Whenever gamma-decay is possible, another process called internal conversion is competing. It is an electromagnetic process, where the nucleus interacts electromagnetically with the atomic electrons, and an electron is emitted instead of the photon (Krane, chapter 10, p. 341). The kinetic energy of the emitted electron is the transition energy minus the electron binding energy

$$T_e = \Delta E - B \tag{1.6}$$

where B is a positive number (even though bound states are negative??). The electron is called a conversion electron, and this electron is high in energy and mathces the gamma-energy. The electron binding energy varies with the atomic orbital (Krane), and the electrons emitted following internal conversion are in a spectrum of different discrete energies. The transition energy must be higher than the electron binding energy, and as a consequence, the electron is labelled with the shell that it was emitted from. (remember, n=1=K, n=2=L, n=3=M, n=4=N)

In the case of the decay of ^{193m}Pt, internal conversion is highly favoured instead of gamma-decay (the intensity of the gammas are very weak). The total decay probability is the summed decay probability for gamma-decay and internal conversion

$$\lambda = \lambda_\gamma + \lambda_{IC} \tag{1.7}$$

and the internal conversion coefficient α can be defined as

$$\alpha = \frac{\lambda_{IC}}{\lambda_\gamma} \tag{1.8}$$

High values of α indicates high probability of internal conversion, relative to probability of gamma-emisson, but the coefficient diverges towards infinity when λ_γ reaches towards zero, which for instance is when the gamma-transition is zero. In general, the coefficient increases as Z^3, which will give a much greater coefficient for heavy nuclei than for lighter nuclei. In addition the coefficient decreases rapidly (ca. $E^{-2.5}$) with increasing transition energy. The multipole order also affects the coefficient, where a higher multipole order indicates a higher value. For higher atomic shells than the K shell (n=1), the coefficient decreases like n^{-3} (Krane, chapter 10, p. 346).

In therapy, the most important process is the process which occurs after the release of the conversion electron. There is a vacancy in the shell where the conversion electron was emitted, and an electron from a higher shell drops down to this energylevel, with the release of an X-ray with an energy equal to the difference between the energy state of the two shells, ΔE.If the transition is an electron from an L shell drops to K shell, and an electron from the L shell is ejected, the processes is called a KLL transition, and the energy of the auger electron is $E_{auger} = E_K - E_{LL}$ (Prasad A. Naik, in Encyclopedia of Spectroscopy and Spectrometry, 1999)https://www.sciencedirect.com/topics/chemistry/auger-process. If the vacancy is filled with an electron from the same shell (or subshell) but the ejected electron is from another shell, the electron is called a coster-kronig electron (like LLM, electron vacancy is moving from L to L and electron in M is emitted), and if the whole process occurs in the same shell, it is called a super coster-kronig process (MMM)

The energy of the X-rays are lower in energy than the gamma-rays, typically. If one of the X-ray photon interacts within the atomic electrons (via photoelectric effect), the electron (which is called an auger electron) will be emitted with the energy of the X-ray minus the atomic binding energy (Handbook of NUclear chemestry, p. 390)

$$T_{a.e.} = \Delta E_{x-ray} - B \tag{1.9}$$

From the vacancy from the auger electron, a new electron can take this place and release another X-ray. The auger electron can cause further ionizations in the atom, either by interaction it self, or from X-rays following the de-exication of another atomic electron by the vacancy. Thus it is possible to have a cascade of electrons and X-rays. The secondary electrons caused by the auger electron can lead to a cascade of new short-range electrons and X-rays, which are typically have ranges of nm in tissue (Handbook of nuclear chemistry p. 2203). Since the X-ray energy is in the low energy region, the auger electrons have low energies (from equation 1.9).

Since auger emitters are short range, they are very precise, and do only harm when bound to DNA or when incorporated into the cellular nucleus (handbook of nuclear chemistry, o. 2204), which means that no neightbooring cells will be affected.

After IC-process, vacancy is produced in an inner atomic shell (n) or subshell (like l=spdf). Vacancies in inner atomix orbitals are unstable, filled by electrons from higher energy levels. 4 processes, radiative X-ray transition, non-radiative transitions of auger, Coster-Kronig and super Coster-Kronig. move primary vacancies to higher shells or subshells. The non-radiative transitions involves multiplication of vacancies in the higher shells and subshels since two new vacancies are produced for each filled vacancy. Whenever energetically possible, super CS transitions dominate the other types. Thus the inner shell vacancies move upward to the valence and near valence shells of the atom, copious emission of electrons occur. Since the transition energies are very small for the higher shell transitions, the electrons ejected possess very small energies and is extremely short range (few nm) in biological matter, find a citation here, numb 8 in chapter.

Energy loss of low E auger electrons. In this energy region, is due to collision loss, not bremsstrahlung. Deflects frequently due to low mass, and the max energy loss is $T_e/2$ per collision.

General stuff ^{193m}Pt: Cellular nucleus is approximately 6μm, while thickness of DNA is ca 2 nm (wikipedia). [9]. Range of the electrons from the decay is between 3.29nm-231μm, according to simulation done by Howell (1992), so well within cellular nucleus. In its decay, it emits 26.4 coster-konig and auger electrons (energy realeased per decay: 10.353 keV) and internal 3 conversion electons (energy released per decay: 126.738 keV). According to the simulation, an additative 12.345 keV is for X-ray energy deposition per decay.

Production: there are multiple ways that this isomer can be produced, either in a neutron field in a reactor, or in a charged particle accelerator like a cyclotron: ^{192}Pt(n,γ) or via ^{192}Os(α,3n). One of the issues with production is that 193mPt (and 195mPt) are difficult to produce with high specific activity (Qaim 2016), and are not well investigated. This study gives an examination of a new route. Many reasons, reactors are on their way out, and Osmium is a poisoneous and difficult target to work with, so using iridium as target is easy, (expensive though?) and the production of radionuclides below iridium is evidently in this work and in papers tarkanyi et al (2006,2019) low.

By itself, not useful for imaging. 191Pt and 195mPt can. Can replace stable N with 13N, but the half life is so short that the radionuclide can not image the distribution it self, so not as a theranostics pair?? or does cisplatin distribute so fast within the body?

Pt-poisoning

[9] https://sci-hub.tw/https://doi.org/10.1118/1.596927

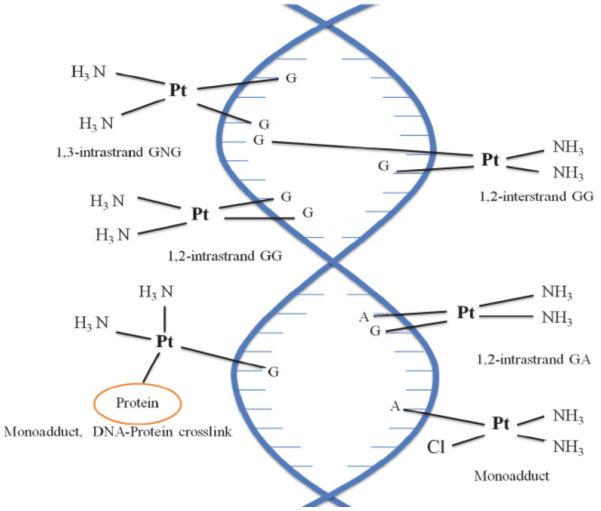

Figure 1.5: A DNA Repair Protein BRCA1 as a Potentially Molecular Target for the Anticancer Platinum Drug Cisplatin - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Common-cisplatin-DNA-adducts-and-functions-For-instance-the-platination-of-human-serum$_fig2_21919257$[$accessed 12 Apr$, 2020].

Chapter 2

General nuclear reaction theory

paragraph based on special curriculum Medical radionuclides can be produced directly using charge particle (cyclotron) or neutron beams (reactors), or indirectly using radionuclide generators or fission (reactor). Medical radionuclides are typically produced in reactors, cyclotrons or by a longer lived-parent decaying into a short-lived daughter in a radionuclide generator system. In general, the production should be cheap, available. Today many radionuclides are only produced in reactors, which is the main source of neutrons, and with reactors aging (Chai Hong Yeong, Mu hua Cheng, and Kwan Hoong Ng. Therapeutic radionuclides in nuclear medicine: Current and future prospects. Journal of Zhejiang University: Science B, 15(10):845–863, 2014.), we need alternative routes to produce critical radionuclides. Cyclotrons have many benefits, like size so that it can be produced directly at the site of usage. One of the major disadvantages is that there is a need to enriched targets to get the desired reaction, and those can be very expensive. Along with high beam intensity the melting of the target can give challenges, so target cooling technqueis need to be there.

In order to create isotopes, nuclear reactions need to occur. There are many different production routes available for a single radionuclide, which is dependent on multiple factors such as choice of target, incident particle-beam and beam energy. To each reaction route, there is an corresponding excitation function which tells us how probable the reaction channel is at various energies. The nuclear reaction data is very important for the optimization of the product, achieving minimal level of isotopic impurities and maximum yield (S M Qaim, R Capote, and F Tarkanyi. Nuclear Data for the Production of Therapeutic Radionuclides. Trs 473, (473):395, 2011., p. 3).

Isotopic purity is important as it is impossible to separate isotopes of the same element (Syed M. Qaim. Nuclear data for production and medical application of radionuclides: Present status and future needs. Nuclear Medicine and Biology, 44:31–49, jan 2017.). An undesired radionuclided can lead to undesired dose to healthy tissue, and a non-radioactive nuclide may lead to poisoning (if large amounts injected), but it will not have any therapautic effect. This is especially important when working with poisoneos elements such as platinum. The only option to minimize isotopic impurities is to choose an appropritate energy window.

Using charged particles instead of neutrons allows for measurement at multiple energies as the particle energy degrades in the foils. The neutron energy is not degraded in the same way, due to electric neutrality, thus can only give cross section at one single energy.

2.1 Nuclear reactions and reaction cross sections

A nuclear reaction occurs when a collision between two nuclei or a nucleus and a subatomic particle takes place. Collision between an accelerated subatomic particle or small nucleus and target nuclei is common in isotope production. A nuclear reaction is denoted as

$$X(a,b)Y \tag{2.1}$$

where X is the target, a is the incoming projectile, b is the outgoing decay channel and Y is the product of the nuclear reaction (Krane, chapter 11.1). There are multiple processes which can occur,

radiative capture is the process where a particle is captured and a γ-ray is emitted in a (x,γ) process. If the incoming and outgoing particle is the same, it is a scattering process, where elastic scattering leaves the target nucleus in the energy same state, and inelastic if the target nucleus is in an excited state. In these type of experiments however, we are interested in emission of particles to create products in which we can measure the reaction cross section.

In a nuclear reaction, the total energy and linear momentum, proton and neutron number, angular momentum and parity are conserved quantities (assuming no meson formation) (Krane, p.380). In the low energy-region in which isotope production typically takes place (¡80 MeV?), compound nucleus reactions take place, where an incoming particle and target nucleus merges by sharing the kinetic energy on all nucleons, and particle emission takes place to reduce the excess energy. [1]Involves nucleon nucleon interactions, lead to a complete therman equlibrium inside the CN. Releases energy by emission of neutrons, protons, alpha particles and gamma rays. A consequence of equilibrium is that the decay of CN should not depend on the way it was formed. "forgets" in all the collisions. Consequently, the decay of the compound nucleus depends only on the mass and atomic numbers, excitation energy and angular momentum. The contrary are direct reactions, where an incoming particle interacts (over such a short time period) so that the incoming particle only interacts with one single nucleon, typically on the surface of the target nucleus. Angular distributions of direct reaction products are sensitive to the momentum transfer and parity change during the reactions. Thus based on the selection rules from angular momentum and parity conversion the angular distribution measurements in direct reactions yield spin and parities of states populated in the exit channel.

The cross section for a reaction can be divided into the cross section of the formation of the compound nucleus via interaction with the incoming projectile a, and the probability that the compound nucleus decay by decay channel b. The total reaction cross section is thus the sum of all the different reaction channels (Handbook of nuclear chemistry, p. 157 (nuclear reactions)),

$$\sigma = \sum_b \sigma(a, b) \tag{2.2}$$

where b can be multiple particles. The general equation which is used to calculate cross sections in this experiment (solving equation 2.24) is the following equation

$$\sigma(E) = \frac{A_0 \cdot t_{\text{irr}}}{N_T \cdot \Phi(E)(1 - e^{-\lambda t_{\text{irr}}})} \tag{2.3}$$

where A_0 is the end of beam activity of the resulting product nucleus (Y), t_{irr} is the irradiation time, N_T is the number of target nuclei (X), $\Phi(E)$ is the projectile flux or current (a), and λ is the decay constant of the product nucleus.

The compound nucleus model (Bohr, 1936) is a model which describes the formation of a compound nucleus by absorption of an incoming projectile by a nucleus close enough to interact with the strong nuclear force, and the decay of the compound nucleus. The kinetic energy shared between the incoming projectile and the nucleon which was struck leads to multiple collisions with other nucleons and rapid exchange of energy. The energy is distributed throughout the nucleus, leaving the original nucleus in an highly excited state. The average energy per nucleon is not sufficient to overcome the binding energy of the nucleus, but due to the statistical distribution in energies there is a probability that one or more nucleons may get sufficient energy to escape the nuclear potential (Krane, chapter 11.10, p. 416). This is decay of the compound nucleus, and this will lower the excitation energy. We can include the formation of the compound nucleus in the nuclear reaction as

$$X + a \rightarrow C^* \rightarrow Y + b \tag{2.4}$$

where C^* is the excited compound nucleus (Krane, chapter 11.10, p. 416)

[1]blue text:https://web-docs.gsi.de/ wolle/TELEKOLLEG/KERN/LECTURE/Fraser/L24.pdf

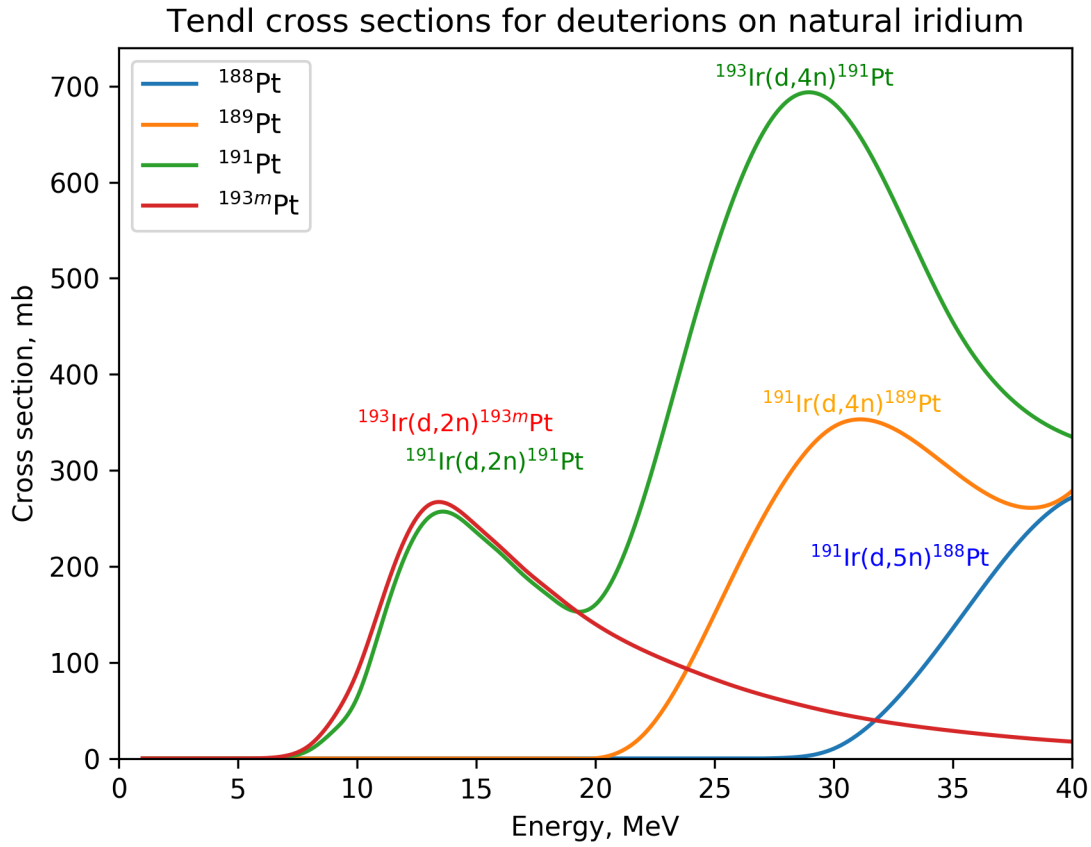

Figure 2.1: Reaction cross sections provided by Tendl for the reactions ^{nat}Ir(d,x)^{188,189,191,193m}Pt

For each possible decay channel of the compound nucleus, there is an associated probability or cross section, which is dependent on the energy of the incoming projectile. A function which evaluates the various cross sections at different energies is called an excitation function. In figure 2.1, the excitation function of the reactions channels for the platinum isotopes ^{188,189,191,193m}Pt resulting from deuterons on natural iridium is plotted (using TENDL nuclear reaction code cite). Natural iridium consists of two stable isotopes, ^{191}Ir (37.3% abundance) and ^{193}Ir (62.7% abundance). ^{193m}Pt can only be produced from ^{193}Ir, ejecting 2 neutrons in the process, which can be denoted as ^{193}Ir(d,2n)^{193m}Pt (^{193}Pt is the compound nucleus formation of deuteron on ^{191}Ir, which has a low production cross section). The other platinum isotopes can be produced as ^{191}Ir(d,2n)^{191}Pt or ^{193}Ir(d,4n)^{191}Pt, ^{191}Ir(d,4n)^{189}Pt or ^{193}Ir(d,6n)^{189}Pt and ^{191}Ir(d,5n)^{188}Pt or ^{193}Ir(d,7n)^{188}Pt. For each reaction route possible, there is a local maximum for the specific route, hence, ^{193m}Pt has only one maxima, and the other platinum isotopes has two. The desired particle emission is energy dependent, and the higher energy provided to the compound nucleus, the probability that more particles will be emitted is higher (Krane, chapter 11.10, p. 419). When a specific isotope is desired, the excitation function can tell us which energy window that maximizes the production and most importantly minimizes particularly other isotopes of the same element, due to the difficulty of separating same chemical elements.

2.1.1 Constraints in nuclear reactions

The potential energy of a nucleus is the sum of the attractive well from the strong nuclear force and the repulsive Coulomb barrier which acts repulsive between charged particles and the nucleus, acting long range (p. 152, Handbook of nuclear chemistry). The radius of the potential well is up to a few femtometer. For a positively charged particle induced nuclear reaction, the energy of the particle should exceed the barrier, or there will be an elastic scatter. However, there is a chance of tunneling,

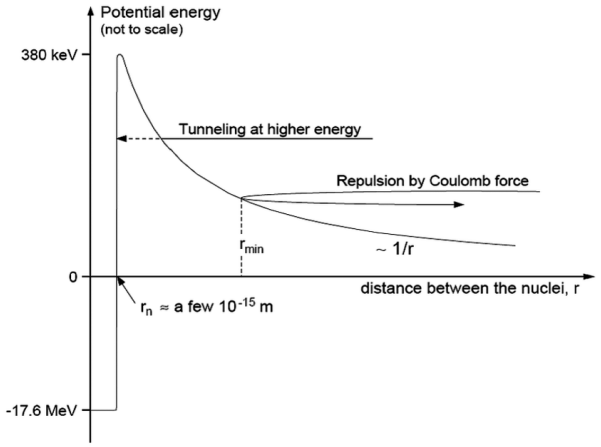

Figure 2.2

which drops with a factor 1/r where r is the distance from the center of the nucleus (Handbook of Nuclear Chemistry, chapter 3 - Nuclear Reactions, section, 3.2.3). The barrier also constraints the emission of particles for a decay channel of the compound nucleus, as the energy for an outgoing decay channel of positive particles must exceed the barrier. There is also a centrifugal barrier, which is dependent on the orbital angular momentum of the the nucleus. However, this barrier is more important in

The height of the Coulomb barrier is dependent on the radius and charge of the incoming or outgoing particle a and the target nucleus b.

$$U_{\text{Coulomb}} = \frac{1}{4\pi\epsilon_0}\frac{e^2 Z_a Z_b}{r_a + r_b} \tag{2.5}$$

In addition, there is a centrifugal barrier, which can constraint some of the incoming particle energy in rotational energy, which depends on the angular momentum of the incoming particle and and the nucleus??? (handbook of nuclear chemistry p. 155.)

$$U_{\text{centrifugal}} = \frac{\hbar\ell(\ell+1)}{r^2} \tag{2.6}$$

The sum of the barriers are the total barrier but the Coulomb barrier is the most important.
In a nuclear reaction, the mass-energy is conserved, which is denoted as the Q-value. The reaction Q-value is the difference is masses between before and after the nuclear reaction occurred (Krane, chapter 11.2). It is defined as

$$Q = (m_i - m_f)c^2 = (m_X + m_a - m_Y - m_b)c^2 \tag{2.7}$$

where m_i is the initial mass, m_f is the final mass and c is the speed of light. If $Q > 0$, then the reaction is exoergic, which means that energy is released in the reaction. There is no threshold energy of the projectile required for the reaction to occur, if only the projectile is present the reaction can occur. If $Q < 0$, then the reaction is endoergic, which means that the kinetic energy of the incoming projectile is converted into nuclear mass or binding energy. For endoergic reactions to occur, there is a minimum threshold energy of the projectile in order for the reaction to happen, which is defined as (Krane, 11.2, p. 382)

$$E_{\text{threshold}} = (-Q)\cdot\frac{m_Y + m_b}{m_Y + m_b - m_a} \tag{2.8}$$

The energy threshold thus depend on the Q-value, the Coulomb barrier for charged particles, and the centrifugal barrier if angular momentum $\ell \neq 0$. The parity though depend, even numbers of ℓ mix with even, and odd with odd (Handbook of Nuclear Chemistry, chapter 3Nuclear Reactions, section, 3.2.3). This gives an indication on when a reaction can energetically occur, but does not tell us how probable the reaction is.

The binding energy is the mass-difference between the nucleus as a whole, and the number of protons and neutrons added

$$B = c^2(z \cdot m_p + n \cdot m_n - m_N) \tag{2.9}$$

where z is the number of protons, n is the number of neutrons, m_p is the proton mass, m_n is the neutron mass, M_N is the mass of of the nuclide, which is the number of nucleons A minus the number of electrons, $M_P = m_A - z \cdot m_e$ (the electronic binding energy per electron is excluded). From Krane's derivation of the nuclear binding energy (Krane, chapter 3.3, p. 65).

From equation 2.7, the larger the mass of the outgoing decay channel, the more negative the Q-value will be. Protons (+1 charge) and neutrons (neutral) are the simplest decay channels of the compound nucleus, each carry a spin of 1/2, with masses m_p = 938.28 MeV/c^2, and m_n = 939.57 MeV/c^2. Combinations like deuterons (d=1p+1n, charge +1) has a mass difference of Δ =2.2 MeV/c^2 from realising 1 proton and 1 neutron separately, a triton (t=2n+1p, charge +1) with Δ = 8.5 MeV/c^2, 3-Helium (^{3}He=1n+2p, charge +2) with Δ = 7.7 MeV/c^2 and alpha-particle (α=2n+2p, charge +2) with Δ = 28.3 MeV/c^2. Thus, Q-values are higher in value, the lighter the particle is. However, in this work, we can clearly see that protons, neutrons and alpha-particles are strongly fed decay channels, while the other don't even appear. The suggested reason for this is that due to blablabla nuclear physics stuff, like shell structure, protons and neutrons are favoured, but since the alpha-particle has such a large binding energy, this channel is also favoured.

2.1.2 Deuterons and stopping power

The deuteron consists of a neutron and a proton, and is the simplest bound state of nucleons. Nucleons have an average binding energy per nucleon of 8 MeV. The detuteron with an observed mass value of 2.224 MeV (Krane, p. 81) is a weakly bound. Thus little energy required to break up the deuteron. Something to keep in mind.

The stopping power of a deuteron beam running through forms the Anderson & Ziegler:

(Techinque nuclear and particle physics p. 30-31) Range: How far will particles penetrate before they lose all there energy. Moreover, if assume that the energy loss is continous, this distance must be a well defined number, the same for alll identical particles with the same initial energy in the same type of material. This quality is called the range of the particle, and depends on the type of material, the particle and its energy. Experimentally the range can be determined by passing a beam of particles at the desired energy through different thicknesses of the material in question and measuring the ratio of transmitted to incident particles. For small thicknesses all the particles manage to pass through. As the range is approached this ratio drops. The surprising thing however is that the ratio does not drop immediately to the background level as expected of a well defined quantity. Instead the curve slopes down over a certain spread of thicknesses. This result is due to the fact that the energy loss is not continous, but statistical in nature. Indeed two identical particles with the same iniitial energy will not in general suffer the same number of collisions and hence the same energy loss. A measurement with an ensemble of identical particles therefor will show a statistical distribution of ranges cented about same mean value. This phenomenon is known as range straggling. In a first approximation this distribution is Gaussian in form. The mean value of the the distribution is known as the mean range and correspond to the midpoint of the corresponding slope. This is the thickness at which roughly half of the particles are absorbed. More commonly however what is desired is the thickness at which all the particles are absorbed, in which case the in which case the point at which the curve drops to the background level should be taken. This point is usually the tagent to the curve at the midpoint and extrapolating to the zero level. This value is known as the extrapolated or practical range

Energy straggling: the energy loss distribution: (instrumentation p. 49) Discussion of energy loss so far has been concerned with mean energy loss suffered by charged particles when passing through a thickness of matter. For any given particle however, the energy lost will not be equal to this mean value because of statistical fluctuations which occur in the number of collisions suffered and in the energy transferred in each collision. An initially monoenergetic beam will therefor show a distribution of energy rather than a delta function peak shifted down by the mean energy loss given by the dE/dx formula after passing through a fixed thickness of material.. see if more necessary?

2.2 Nuclear reaction models

The optical model (proton/neutron, and alpha/deuteron), gamma strength function.

EMPIRE 3.2.3

CoH 3.5.3

ALICE 2017

TALYS 1.9

TENDL 2019

2.3 Detection and identification of radionuclides

Gamma-ray spectroscopy is a method to identify and obtain information about radioactive nuclei present in a detector. As beta and alpha decay can result in an excited daughter product, the spectrum in fact shows the de-excitation of the daugher product. Since we know that these gamma-lines are transitions which happens right after a beta or alpha decay (or isomer transition), we identify the parent with gamma-ray spectroscopy. A detector has channels in which counts are regiserted. These channels are ... similar to the gamma-ray energy. Thus a spectrum has channels (which increases in energy) along the x-axis and and counts along the y-axis. If a detector registers many counts, it means that the state is highly populated, and the intensity of the gamma is strong (Krane, p. 351).

2.3.1 Radioactive decay law

From here based on Krane chapter 6 [2]

The activity of a nucleus is defined as the number of decayed nuclei per unit time of a radioactive product, which is equal to the radioactive decay rate

$$A = \frac{dN}{dt} = -\lambda N \tag{2.10}$$

where N is the number of nuclei, t is the time and λ is the decay constant. Solving equation 2.10 gives number of decayed products at time t

$$N(t) = N_0 e^{-\lambda t} \tag{2.11}$$

Since $N \propto$A, the relations $\frac{N_0}{A_0} = \frac{N(t)}{A(t)}$ are valid, and we can rewrite the equation 2.11 to

$$A(t) = A_0 e^{-\lambda t} \tag{2.12}$$

This accounts for single nucleus decaying into a daughter product, without anything first decaying into the parent nucleus. However it is common that a radioactive nucleus decays into another radioactive nucleus. Hence the daughter activity will increase due to feeding from the parent. For multiple decay, Bateman equation is used describing the activity in nucleus n of the decay chain (Voyles2018, which article??)

$$A_n = \lambda_n \sum_{i=1}^{n} \left[\left(A_{i,0} \prod_{j=i}^{n-1} \lambda_j \right) \cdot \left(\sum_{j=i}^{n} \frac{e^{-\lambda_j t}}{\prod_{i \neq j}^{n} (\lambda_i - \lambda_j)} \right) \right] \tag{2.13}$$

where A_n is the activity of nuclei n in the decay chain, with the corresponding decay constant λ_n. The equation sums over all nuclei in the decay chain. $A_{i,0}$ is the initial activity of nucleus i, and j is the nucleus which is feeding into nucleus i.

[2] https://faculty.kfupm.edu.sa/phys/aanaqvi/Krane-Ch-6.pdf

If a target of stable nuclei is assumed, which is exposed to a particle beam which induces various nuclear reactions, the constant rate of production of a specific reaction is dependent on the number of target nuclei, the current of flux of the particle beam and the reaction cross section

$$R = N_T \Phi \sigma \tag{2.14}$$

where R is the production rate, N_T is the number of target nuclei, Φ is the beam current or flux and σ is the reaction cross section. In the assumption of the production rate being a constant value, the number of transformed target nuclei is small in comparison to the total number during the irradiation time. The number of produced nuclei from a specific reaction per unit time is thus thus the produced nuclei minus the decayed nuclei (activity)

$$dN = Rdt - \lambda N dt \tag{2.15}$$

which has the solution

$$N(t) = \frac{R}{\lambda}(1 - e^{-\lambda t}) \tag{2.16}$$

From equation 2.10, the total activity produced during irradiation time t is thus

$$A(t) = R(1 - e^{-\lambda t}) = N_T \Phi \sigma (1 - e^{-\lambda t}) \tag{2.17}$$

At the end of beam, the activity is denoted as A_0, and t is the irradiation time:

$$A_0 = N_T \Phi \sigma (1 - e^{-\lambda \Delta t_{\text{irr}}}) \tag{2.18}$$

When a target is irradiated, the activity of the product nucleus will increase until secular equilibrium is achieved, which is when the product rate and decay rate are constant. Hence it is not necessary to irradiate a target for more than 2-3 half lives.

If a spectrum is counted at a delay time Δt_d after end of beam with a counting time Δt_c the total number of decayed products are

$$N_D = \int_{\Delta t_d}^{\Delta t_d + \Delta t_c} A(t) dt \tag{2.19}$$

Using equation 2.12 for A(t), the solution to the above equation is

$$N_D = \frac{A_0}{\lambda} e^{-\lambda \Delta t_d}(1 - e^{-\lambda \Delta t_c}) \tag{2.20}$$

which again is equal to

$$N_D = \frac{A(t)}{\lambda}(1 - e^{-\lambda \Delta t_c}) \tag{2.21}$$

We can only know the number of decayed products which are detected. This is dependent on the efficiency of the detector, the intensity of the gamma-rays and the true number of decayed products

$$N_C = N_D \epsilon I_\gamma \tag{2.22}$$

where N_C is the number of observed/counted gamma-rays, ϵ is the efficiency of the detector and I_γ is the gamma-ray intensity.

Thus, we can obtain an expression for $A(t)$ after a delay time:

$$A(t) = \frac{N_C \lambda}{\epsilon I_\gamma (1 - e^{-\lambda \Delta t_c})} \tag{2.23}$$

Again using 2.12 for A(t), the above expression can be rewritten using A_0 and the delay time Δt_d

$$A_0 = \frac{N_C \lambda}{\epsilon I_\gamma (1 - e^{-\lambda \Delta t_c}) e^{-\lambda \Delta t_d}} \tag{2.24}$$

2.3.2 High purity Germanium detector

High purity Germanium detector is a type of semiconductor, which is a material where the energy required to remove an electron from the valence band (in the outer atomic shell) to the conduction band is small. The germanium atom has atomic number 32, and 4 valence electrons in the outer p4 shell (need citation?). The atoms in the detector are bound through covalent bonds in a crystal structure. The main mechanism of a semiconductor is creation of electron-hole pairs after energy deposition of an ionizing particle in the crystal. If an electron is excited to the conduction band, a hole is left. This hole can move as a neighboring electron fills this spot, and it can cause a chain reaction, and the hole will move in the crystal. Both the electron in the conduction band and the and the hole in the valence band contributes to an electric current. Under influence of an electricfield, the electron-hole pairs will be collected and we can measure the incident as a count. The major advantage with semiconductor detector is that the average energy to create an electron-hole pair is very low, which results in a superior energy resolution in comparison to other detectors like gas and scintillation detectors. High energy resolution advantageous in gamma-ray spectroscopy which makes it possible to separate to gamma-ray peaks within less than a keV. At room temperature, thermal energy can excite the electron from the valence to the conduction band and cause noise in spectra. Therefor, Germanium detectors are operated at 0 Kelvin. Write about recombination and trapping, noise, np semiconductor junction, depletion depth?? (Techniques for Nuclear and Particle Physics Experiments, William R. Leo, p. 215-216).

Ideally, for all gamma-rays with the same energy, should be detected in the same channel giving a step function. However, realistically, the resolution of a detector is not that good, and instead of seeing a delta peak, the peak is typically gaussiam shape with a finite width. The full width half maximum ΔE of the peak tells us how well the relative resolution at gamma-energy E,

$$\text{resolution} = \frac{\Delta E}{E} \tag{2.25}$$

The energy resolution is important, as it tells us how well it can distinguish two close lying peaks from each other (Techniques of Nuclear and particle Physics.. , p. 117). The resolution of a germanium detector very good (0.1% for a 1 MeV gamma-ray) in comparison to for instance NaI detector (8-9% for a 1 MeV gamma-ray) (Techniques of Nuclear and particle Physics.. , p. 117). explain why, prob in semiconductor chapter!

The peak it self is not directly gaussian. Ionizing radiation statistics is based upon Poisson statistics, where and the probability of observing N events is a discrete value

$$P(N) = \frac{\mu^N e^{-\mu}}{N!} \tag{2.26}$$

where μ is the mean value. This distribution counts when the probabiliy is a small (eg decay prob?) value and that the total number of trials are large (number of decays) (Techniques of Nuclear and particle Physics.. , p. 85). For poisson distribution, the average is equal to the variance; $\sigma^2 = \mu$. From there, the standard deviation (σ) is thus equal to the squareroot of the average.

The distribution is not symmetric, but as μ increases in value, the peak approxes a gaussian shape. The total number of counts is the area of the peak. The total peak is a Guassian assumption but with an exponential skew towards kiw E caused by incomplete charge collection, abd a step function for taking compton backgroun into account.

In calculation of the peak area, there are two uncertainties of relevance, the relative statistical uncertainty in the counting from the Poisson statistics,

$$\sigma N_i = \sqrt{N_i} \tag{2.27}$$

If numb of counts $N_i = 10000$, the relative uncertainty ($\frac{\sigma N_i}{N_i} = \frac{1}{sqrtN_i}$=1%). Therefor we say that a good number of counts is 10000 or more to reduce the statistical uncertainty. The other is systematic in the detector, and can for instance be due to a process called annealing, which is heat damage to

the detector. Can fix by taking a blanket of resistor wrap crystal in, rise to high temp, let it sit and slowly deheat to room temp, traps will defuse and detector is repaired (this is notes from Andrew).

Also write about deadtime!

2.3.3 Gamma-ray spectrum

Spectrum: consists of photopeaks, a compton continuum, compton edge, backscatter peak, single exscape double escape. In cases where positrons exist, chances of having a broad fat 511 keV peak.

Germanium detecors, highest resolution for gamma-rays, from frew keV to 10 MeV. The peak to Compton ratio is much greater due to the higher photoelectric cross section of Germnaium . The largets challenges are with signal to noise ratio, it is important to shield very well to minimze background radiation (Techniques for Nuclear and particle..... William R. Leo, p. 241).

here from another citation: "Practical Gamma-ray Spectroscopy". Gordon R. Gilmore. Nuclear Training Services Ltd Warrington UK. (can be find under articles in masterthesis). This book can also be used in particle interaction in matter check!! In a detector, the particles interacts as the photons described in particle interaction, via photoelectric, compton scattering and pair production. Photoelectric absorption where the photon is completely absorbed by atomic electron is desired because all of the energy is deposited within the detector. For a compton scattering event, if the resulting photon's energy is also deposited in the detector (for a large detector), then the total energy would add up. Same for pair production. The photon must interact in the detector volume, and the resulting electron and positron energy is deposited in the detector volume. However when the positron slows down, it annihilates with one atomic electron, releasing two 511 keV photons. If both annihilation photons's energy is deposited in the detector volume this will also contribute to a full width peak. If one 511 photon escape and the other is deposited, there will be a peak at $E_\gamma - 511$ keV, and if both peaks escape, there will a double escape peak at $E_\gamma - 1022$ keV. The "degree of incomplete absorption" depends upon the size of the detector and the gamma-ray energy. As previously discussed photoelectic effect dominates at low energies, and the less compton scattering and of course pair production (for E gamma higher than the threshold.). The detector size also matters because the larger the more room for the photon to scatter in and lose energy before escaping. (p. 32)

The total spectrum can be seen on p. 33 in the book. Pile-up is done because of random summing, determined by the statistical probability of two gamma-rays being detected at the same time and therefor on the sample count rate.

Interaction with detector shielding: Photoelectric effect can be followed by emission of characteristic X-ray of the absorbing medium. X ray can escape the shielding and be deteced by the detector. Compton scattering: most gamma rays are scattered through the a large angle by the shielding, BACKSCATTERED. Whatever the initial enervy was (if scattered by more than 120 degrees) are within 200-300 keV. Peak appears as broad. Pair production: annihilation peak (511 peak) caused by the escape of one of the 511 keV photons from the shielding following annihilation of the pair production positron. Analogous to the single and double escape mechanisms within the detector but only on 511 keV photons can ever be detected since they are emitted in the opposit direction. So in order to have a 511 peak, energy of gamma ray must be more than 1022 keV. (p. 34-35).

The 511 peak can also be expected when postron emitters are present since beta + particle interacts with electron.

Since Compton scattering can be in a spectrum of energies, the gives rise to a Compton continuum, before the gamma-ray escapes the detector.

The shape of the peak: The peak is a histogram that approximate a Gauss curve (p. 186). Peak searching (SAMPO) using first and second order derivatives to search for peaks (p.185) Due to incomplete charge collection (that electron or holes are not collected) no matter how caused moves counts from the centre of the Gaussian distribution to lower channels, creating a low energy tale to the peak (p.135).

Include a picture of peak shape and gamma-ray spectrum!! from the same book