Stopping Power in Ion-beam Therapy and Biology

Bragg additivity, collective excitations, and wakes

Ceferino Obcemea

Radiation Research Program
National Cancer Institute, Bethesda, MD, USA
obcemeach@nih.gov
Disclaimer

This talk is based solely on the author’s opinion and does not reflect that of NCI as an institution.

I have no conflicts to report.

2. Bethe-Bloch formulation of the Coulomb scattering process.

3. Bethe-Bloch + Bragg additivity to calculate tumor dose in ion–beam therapy (p$^+$ or C$^6^+$).

4. Identify 4 Open Questions: what happens in the microscopic regime when physics meets biology?

5. Proposal: Reframe Stopping Power via the Lindhard dielectric function

Background materials:


... pending 2022 ?: P. Sigmund, “Particle Penetration and Radiation Effects Volume 3: (collective effects, wakes)
Stopping Power $Sp = -\frac{dE}{dx}$ is the **energy imparted** by a charged particle incident on a target medium of thickness $dx$. 

Mathematically, it is defined as:

$$\left. -\frac{dE}{dx}\right|_{E=E_1} = -\lim_{\Delta x \to 0} \frac{(E_1 - E_0)}{\Delta x}$$
In ion-beam therapy, we choose the beam energy so that the tumor gets located in the Bragg peak.
How does Stopping Power relate to Dose?

Dose = \( \frac{dE}{dm} \) is energy absorbed by the medium per given mass.

If we divide the stopping power by the density of the medium, we arrive at mass stopping power \( \frac{S}{\rho} \).

\[
\text{Dose} = \frac{dE_{el}}{dm} = \int \Phi(E) \frac{S_{el}}{\rho} \, dE
\]

where: \( \Phi \) is fluence at energy \( E \).
The unit is J/kg or Gy.
The most commonly-used formulation of the Coulomb scattering process is the Bethe-Bloch equation:

\[ -\left( \frac{dE}{dx} \right) = \frac{4\pi}{m_e c^2} \cdot \frac{n z^2}{\beta^2} \cdot \left( \frac{e^2}{4\pi \varepsilon_0} \right)^2 \cdot \left[ \ln \left( \frac{2m_e c^2 \beta^2}{I \cdot (1 - \beta^2)} \right) - \beta^2 \right] \]

**Bethe-Bloch Equation**

which for the non-relativistic case, simplifies to:

\[ -\frac{dE}{dx} = \frac{4\pi n z^2}{m_e v^2} \cdot \left( \frac{e^2}{4\pi \varepsilon_0} \right)^2 \cdot \left[ \ln \left( \frac{2m_e v^2}{I} \right) \right] \]
In ion–beam therapy, we use Bethe-Bloch + Bragg additivity to calculate tumor dose:

The classical Bethe formula [17,18] describes the energy loss of heavy charged particles traversing matter:

\[
\left( \frac{dE}{dx} \right)_e = -4\pi N \frac{Z_{\text{eff}}^2 e^4}{m_e c^2 \beta^2} Z L
\]

(1)

\[L = \ln \left( \frac{2m_e c^2 \beta^2}{I (1 - \beta^2)} \right) - \beta^2\]

(2)

Following the notation of Schneider et al., the stopping-power-ratio \(\rho_s\) is defined as the energy loss rate in the traversed material \((dE/dx)_m\) relative to the energy loss rate in water \((dE/dx)_w\):

\[\rho_s = \frac{(dE/dx)_m}{(dE/dx)_w}\]

(3)

By combining equation (1) and (3) this results in

\[\rho_s = \frac{N_m Z_m}{N_w Z_w} \cdot \frac{L_m(\beta, I)}{L_w(\beta, I)}\]

(4)

where \(L\) is the logarithmic term of the Bethe formula (2). By introducing the relative electron density \(\rho_e\)

\[\rho_e = \frac{N_m Z_m}{N_w Z_w}\]

(5)

equation (4) can be shortened to:

\[\rho_s = \rho_e \frac{L_m(\beta, I)}{L_w(\beta, I)}\]

(6)

For materials containing more than one chemical element, the electrons per unit mass \(N_g\) and the mean excitation energy have to be calculated from the chemical, composition. The mean excitation energy is derived using the Bragg additivity rule taking into account their fraction of weight \(\omega_i\) [9].

\[\ln(I_g) = \left( \sum \frac{\omega_i Z_i}{A_i} \ln I_i \right) \left( \sum \frac{\omega_i Z_i}{A_i} \right)^{-1}\]

(7)
With Bragg additivity, the mean excitation value of tissues = the weighted sum of mean excitation of their atomic components.

Table 1
Chemical composition and densities for the tissue substitutes. HU-values with the standard error of the mean (SEM) for one scanner setup. The compositions in % of weight are provided by the manufacturer. The elemental I-values were taken from [19].

<table>
<thead>
<tr>
<th>substitute material</th>
<th>density [g/cm³]</th>
<th>HU ± SEM</th>
<th>chemical composition in mass percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>lung (LN300) RMI 455</td>
<td>0.270</td>
<td>-706 ± 1.1</td>
<td>8.46  59.38  1.96  18.14  11.19  0.78  0.10</td>
</tr>
<tr>
<td>lung (LN450)</td>
<td>0.450</td>
<td>-544 ± 0.5</td>
<td>8.47  59.57  1.97  18.11  11.21  0.58  0.10</td>
</tr>
<tr>
<td>AP6 adipose RMI 453</td>
<td>0.943</td>
<td>-99 ± 0.4</td>
<td>9.06  72.30  2.25  16.27  0.13</td>
</tr>
<tr>
<td>BR12 Breast RMI 454</td>
<td>0.980</td>
<td>-53 ± 0.4</td>
<td>8.59  70.11  2.33  17.90  0.13  0.95</td>
</tr>
<tr>
<td>CT Solid Water RMI 451</td>
<td>1.017</td>
<td>-6 ± 0.5</td>
<td>8.00  67.30  2.39  19.87  0.14  2.31</td>
</tr>
<tr>
<td>Water</td>
<td>1.000</td>
<td>0 ± 0.4</td>
<td>11.19  88.81</td>
</tr>
<tr>
<td>SR2 Brain</td>
<td>1.051</td>
<td>15 ± 0.4</td>
<td>10.83  72.54  1.69  14.86  0.08</td>
</tr>
<tr>
<td>LV1 RMI (Liver)</td>
<td>1.094</td>
<td>67 ± 0.4</td>
<td>8.06  67.01  2.47  20.01  0.14  2.31</td>
</tr>
<tr>
<td>IB3 Inner Bone RMI 456</td>
<td>1.152</td>
<td>213 ± 0.5</td>
<td>6.67  55.64  1.96  23.52  3.23  0.11  8.86</td>
</tr>
<tr>
<td>B200 Bone Mineral</td>
<td>1.145</td>
<td>208 ± 0.5</td>
<td>6.65  55.52  1.98  23.64  3.24  0.11  8.87</td>
</tr>
<tr>
<td>CB2 -30% CaCO3</td>
<td>1.333</td>
<td>439 ± 0.5</td>
<td>6.68  53.48  2.12  25.61  0.11  12.01</td>
</tr>
<tr>
<td>CB2 -50% CaCO3</td>
<td>1.559</td>
<td>789 ± 0.5</td>
<td>4.77  41.63  1.52  32.00  0.08  20.02</td>
</tr>
<tr>
<td>SB3 Bone. Cortical RMI 450</td>
<td>1.822</td>
<td>1162 ± 0.8</td>
<td>3.41  31.41  1.84  36.50  0.04  26.81</td>
</tr>
</tbody>
</table>
4 Open questions: (around Bragg peak)

A) What if the target medium can affect the charge state/dressing of incident ion (first Born approx. may no longer be valid).

**Born approximation**

\[
|\psi_k\rangle = |\phi_k\rangle + \xi_0 U |\phi_k\rangle + \xi_0 U \xi_0 U |\phi_k\rangle + \cdots = \sum_{n=0}^{\infty} (\xi_0 U)^n |\phi_k\rangle
\]

- Then, making use of the identity \( f(\theta, \phi) = -\frac{1}{4\pi} \langle \phi_{k'} | U | \psi_k \rangle \), scattering amplitude expressed as **Born series** expansion

\[
f = -\frac{1}{4\pi} \langle \phi_{k'} | U + U G_0 U + U G_0 U G_0 U + \cdots | \phi_k \rangle
\]

- Physically, incoming particle undergoes a sequence of multiple scattering events from the potential.

---

c/o https://www.tcm.phy.cam.ac.uk/~bds10/aqp/lec20-21_compressed.pdf
4 Open questions:

B) $\sigma_s$, $S_p$ for cellular components, DNA, etc. are not known.

Structure of a generalized cell as seen by:

- a biologist
- a chemist
- a physicist
Can $\sigma_S$ of water approximate that of DNA?

Simulation of the physical interactions within the DNA geometry. The physical interactions between the incident protons (including secondary electrons) and the DNA target were simulated with the physical models present by default in Geant4-DNA (version 10.1) and already detailed in the literature\textsuperscript{9,10,12}. The DNA volumes were filled with liquid water, which constitutes an approximation for biological medium, to simulate the physical interactions because the Geant4-DNA models available use interaction cross sections in liquid water only.
4 Open questions:
C) What if Bragg additivity is no longer valid?
4 Open questions:
D) In condensed matter, collective excitations and wakes affect stopping power.


In metals, due to the low binding forces on conduction electrons, collective phenomena must be expected to be noticeable even at moderate projectile speeds. In fact, the term Lindhard function denotes the dielectric function of
DNA as ultimate target of radiation cell damage
Is DNA a conductor, capable of carrying collective excitations (e.g. plasmons)?

What is the band structure of in-situ, hydrated, DNA?
Charge transport in DNA

The base pair stack within double helical DNA provides an effective medium for charge transport.
…recent nanotechnological research has focused on the possible application of DNA duplexes as one-dimensional quantum wires (6–8) and as templates for directed material deposition (9). In the same arena, larger nucleotide assemblies, like crossover junctions, have been used as building blocks for nanoscale structures and signaling devices (10–14). Understanding the molecular mechanisms of charge transport for these nanoscale building blocks is of fundamental importance to designing DNA microarray electronics …

However, when the incident charge is an ensemble of particles, such as in a high-fluence beam, the stopping power can be best described by the dielectric response of the target material, i.e.

\[
\frac{dE}{dx} = S_p = \frac{1}{2\pi^2 v} \int d^3k \frac{k \cdot v}{k^2} \text{Im} \left[ -\frac{1}{\varepsilon(k, \omega = k \cdot v)} \right]
\]

(2)

where \( S_p \) is the proton stopping power, \( \varepsilon \) is the dielectric function of the medium, \( \omega \) is the frequency and \( v \) is the velocity of the projectile. For a cluster of \( N \) ions with atomic charge \( Z_i \) and relative positions \( r_{ij} \), the cluster stopping power [11] is given by:

\[
S_{cl} = \left[ \sum_{i=1}^{N} Z_i^2 + \sum_{i \neq j}^{N} Z_i Z_j I(r_{ij}, \theta_{ij}) \right] S_p
\]

(3)

with \( \theta_{ij} \) as the angle of the vector \( r_{ij} \) and the vicinage function \( I \) integrated over \( \theta_{ij} \) is given by:

\[
I(r, \theta) = \frac{1}{2\pi^2 v S_p} \int_0^\infty \frac{dk}{k} \int_0^{k \omega} dw w \text{Im} \left[ -\frac{1}{\varepsilon(k, \omega)} \right] \cos \left( \frac{wq}{v} \right) J_0 \left( b \left( k^2 - \frac{w^2}{v^2} \right)^{1/2} \right)
\]

(4)

where \( a \) and \( b \) are the orthogonal components of vector \( r \) and \( J_0 \) is the zeroth order Bessel function.
At high-flux, or projectiles as clusters, there is an enhancement of stopping power due to collective excitations in the medium and vicinage effect.

Enhancement of stopping power of 1.6 to 1.8
Resolving the open questions in #4 can:

- Lead to a better understanding of the microscopic physical mechanisms underlying radiation effects (LET, RBE, etc.).
- Account for the actual characteristics (electronic structure, binding, phase) of biological targets.
- Better describe novel particle acceleration schemes (LPA) that can potentially improve cancer treatment outcomes.
In summary:

1. Bethe-Bloch = \( \Sigma \) binary collisions between incident ions and target.

2. Around Bragg peak, Born approx. and Bragg additivity may not be valid.

3. The electronic structure, phase, collective excitations of the target may affect Sp.

4. We need experimental data and/or theoretical guidance to understand Sp of actual biological targets.

5. We seek collaboration with the nuclear physics community on these questions.
I am deeply grateful to Prof. Peter Sigmund for the many instructive and enlightening discussions on stopping power theory and applications, and to my colleagues in the Radiation Research Program at NCI for discussions on biological and clinical aspects of cancer therapy.