Definitions of Radiation Quality for ion-beam therapy

In today’s ion-beam therapy, radiation quality is mainly expressed using Linear Energy Transfer (LET), and only rarely through lineal energy. Generally, the former is estimated through computations, while the latter is derived from microdosimetric experiments. This section focuses on defining the quantities related to these two specifications, deferring to a different chapter for further discussions on their relationship and the methods used to assess them using passive detectors and active microdosimeters. In addition to the formal definitions detailed in ICRU publications, this text aims to characterize the distinct environment of ion-beam therapy, which employs nearly monoenergetic and highly unidirectional beams.

* 1. Definitions

The terminology and quantities related to radiation quality have evolved over time. Some definitions have been modified or adapted, as seen in the different International Commission on Radiation Units and Measurements (ICRU) publications (ICRU 16 vs. ICRU 60) for LET and the description of mean chord length (ICRU 36 vs. ICRU 98). Below is a logically structured list of key radiation-quality quantities.

*Energy deposit:* Referring to a single interaction between an incident ionizing particle (including photons and neutrons) and a target particle, the energy deposit is the difference between the initial energy of the incident particle and the energy of the outgoing particle or particles, considering possible changes in rest energy.

*Energy imparted (є):* Defined within a given volume, where one or more ionizing particles interact with particles in that region, it is obtained by summing all energy deposits within the small volume from primary particles, and secondary electrons and ions. Energy imparted outside the target by high-energy secondary electrons (delta rays) is not included in the calculation. The volume of interest may be the sensitive volume of a microdosimeter or a biological target. In the case the imparted energy refers to single ionizing particle, a subscript 1 is added: *є*1. The actual dimension of the “small” volume is not strictly specified and could range, depending on the application, from nanometric to micrometric size.

*Site size*: Site size refers to a general characterization of the volume of interest, conventionally expressed as a length—typically the diameter in the case of spherical shapes, or an approximate side length for more irregular geometries.

*Specific energy (z):* The ratio of energy imparted to the mass of the small sensitive volume considered. It has the same dimension as dose. In the case the specific energy refers to single charge particles, a subscript 1 is added: *z*1.

*Energy-deposition event:* The process by which energy is imparted through ionization and excitation from a single ionizing particle within the volume of interest, including energy correlated with its secondary electrons. Often referred to simply as an “event”.

*Energy imparted in a single event (*є*₁):* Follows the definition of ε, but restricted to the energy transferred by a single primary charged particle, denoted with subscript 1.

*Single-event specific energy (z₁):* Defined as the ratio ε₁/m, where m is the mass of the volume considered.

*Lineal energy (y):* Estimated as є₁ divided by the mean chord length*l̄*: y = є₁ / *l̄*. The value of *l̄* is computed using chord-length distributions, depending on primary particle trajectories and volume shape. The ICRU 98 report clarifies that *l̄* is determined by accounting for the path of primary particles in the reference volume; for almost-unidirectional beam irradiation in a flat sensitive volume can be approximated by its thickness. Lineal energy is widely used in microdosimetric analyses, though є, z, є₁, and z₁ may also be employed.

*Lineal-energy probability density distribution in frequency f(y) and in dose d(y)*: The element *f*(y) · *dy* represents the probability that in a field, the lineal energy falls in the infinitesimal interval (y, y+dy). Analogously, the element d(*y*) · *dy* represents the fraction of dose delivered by the radiation field in the interval of lineal energy (y, y+dy). The two distributions are normalized so that:

*Frequency and dose-mean lineal energy*: they are calculated as the first moment of the probability density distribution of lineal energy in frequency *f*(*y*) and in dose *d*(*y*):

*Energy lost (dE):* The energy lost by a particle due to electronic interactions, nuclear elastic interactions, or bremsstrahlung radiation. Losses from radiative and nuclear elastic collisions are generally negligible while most relevant is energy loss via electronic interactions, particularly for the energies of ion beams used in therapy.

*Unrestricted Linear Energy Transfer (LET):* Defined as the ratio between mean energy lost in electronic interactions (d*E*) and the traversed distance (d*l*). The mean is calculated considering the energy-loss straggling distribution of identical particles (same type and energy). The term “unrestricted” means that the total energy of secondary electrons generated in the collisions is accounted with no restriction due to escape. Following the originally description of ICRU 16, d*l* should be small enough that multiple electronic collisions are unlikely—for clinical ions, typical d*l* isof the order of 1 nm. A correct evaluation must account that charged particles traversing without interactions have d*E* = 0. The energy lost in electronic collisions by charge particles identical in type and energy is stochastic: LET is the results of the averaging of those energy losses and is, therefore, non-stochastic. The important consequence is that specific particle type and energy the LET is unique. An ideal device for experimental measurement of unrestricted LET would have an exceptionally thin volume (d*l* lower than 1 nm) and at the same time be able to capture the ionizations produced by the most energetic delta rays, whose range could exceed 1 mm for the highest energies of theclinical ion beams. Such detection is extremely challenging. However, if energy loss is negligible compared to the total kinetic energy of the ionizing particle, and interactions other than electronic are negligible, unrestricted LET can be estimated experimentally by measuring the difference between entry and exit energy of the particle in a material of thickness d*l*.

Originally, LET was used as an abbreviation, while the representation of the quantity and its formulas utilized *L*. However, in recent years, LET has been often adopted in clinical publications, becoming the standard notation in discussions related to radiation therapy and dosimetry. For clarity, in the following, the original notation of *L* will be used for the quantity.

*Restricted LET:* Follows the unrestricted LET definition but excludes energy from secondary electrons exceeding a chosen cutoff energy (Δ). For example, LET₁₀₀ excludes secondary electrons with energies > 100 eV, meaning their energy loss is capped at 100 eV. Some definitions completely ignore electrons exceeding 100 eV, which can lead to differences in interpretation. Since 100 eV electrons in water travel only a few nanometers, LET₁₀₀ effectively describes energy loss near the primary particle track.

*Track and Dose Density Distributions of LET*: While LET for a specific particle type and energy is a single value, a typical radiation field consists of thousands of particles with diverse types and energies. This heterogeneity generates a quasi-continuous variation of LET which is naturally described by density distributions in frequency f(L), and in dose d(L).

The distributions are normalized so that:

The element *f*(*L*) · *dL* represents the fraction of particles of the heterogenous field whose LET falls in the infinitesimal interval (*L*, *L*+ d*L*). Analogously, the element d(*L*) · *dL* represents the fraction of dose delivered by the radiation field in the LET interval (*L*, *L*+ d*L*).

*Track-averaged LET (LETt or L̄*T*) and dose-averaged LET (LETd or L̄*D*):* they are calculated as the first moment of the frequency distribution of the LET (restricted or unrestricted) of the dose distribution of the LET (restricted or unrestricted):

In case the average is calculated from a restricted distribution, a second subscript should indicate it, for instance *L̄*T,100.

* 1. Clarifications
* "LET" has become a widely used descriptor of a general radiation property. In ion-beam therapy, LET is increasingly regarded as synonymous with radiation quality and is commonly employed to differentiate types of ionizing radiation into categories such as low-LET and high-LET. This generalization encompasses all ionizing radiation types—for example, X-rays are typically classified as low-LET radiation, even though LET cannot be strictly defined for photons under its formal definition. The threshold between low and high LET is not universally defined. One practical approach is to relate it to the maximum stopping power of electrons in water, which is on the order of 10 keV·µm⁻¹. This threshold is particularly useful from a radiobiological perspective, as the proportionality between cellular damage effectiveness and dose tends to shift around this value. Typically, photons are considered low-LET radiation; protons with energies above 4 MeV also fall into the low-LET category, whereas carbon ions—at all clinically used energies—are consistently classified as high-LET radiation.
* The term LET has become a general description of a radiation property: In ion-beam therapy, LET is becoming almost the synonymous of radiation quality and used as general parameter to distinguish the type of ionizing radiation indicated as low-LET and high-LET. This generalization includes all the ionizing radiation so that, for instance, X-rays are indicated as the typical low-LET radiation, although no LET can be established for photons according to the definition.

The threshold between low and high LET is not univocal. A possible way is to associate it to the maximum stopping power value of the electrons in water (in the order of 10 keV·µm‑1); this is convenient also for radiobiological purposes since it is around that value that the effectiveness on cell damage changes with LET. In general, photons are low-LET radiation, protons with energy exceeding 4 MeV are low-LET radiation and carbon ions are constantly high-LET radiation also for the maximum energies used in clinics.

* In publications related to clinical irradiation fields, the term LET distribution is typically used to describe the spatial *3D distribution of LETd* within or around the target volume. This is distinct from *density distributions of LET*. Both distributions have been often referred simply as LET distribution, inevitably creating confusion and the suggestion is to explicitly emphasized he distinction to prevent any ambiguity.
* When LET distributions and LET averages are discussed in other chapters, the general assumption is that they refer to unrestricted LET, although this may not apply to all reference data in literature, as noted by Kalholm et al.[[1]](#footnote-1)

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1. Kalholm F, Grzanka L, Traneus E, Bassler N. A systematic review on the usage of averaged LET in radiation biology for particle therapy. Radiotherapy and Oncology. 2021 Aug 1;161:211-21. [↑](#footnote-ref-1)