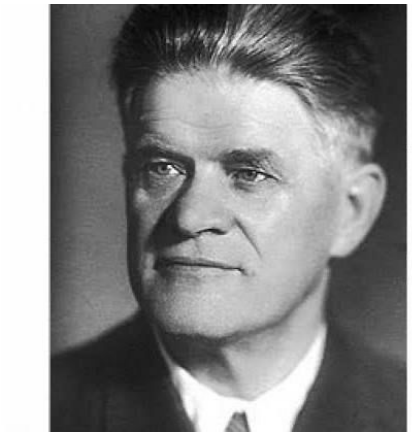
Cherenkov Luminescence Imaging

Key scientists involved

Marie Curie

Marie Curie (1898–1902): Isolated and studied radium and polonium; laid the groundwork for understanding radioactive decay.
Importance: Provided the basis for studying radiation interactions with matter, which later enabled Cherenkov's work.



Pavel Cherenkov

Pavel Cherenkov (1934): Observed a faint bluish glow in uranium salt solutions exposed to gamma radiation.

Ilya Frank

Igor Tamm

Ilya Frank & Igor Tamm: showed that charged particles moving faster than light in a medium emit electromagnetic radiation

Recognition: Nobel Prize in Physics awarded to Cherenkov, Frank, and Tamm in 1958.

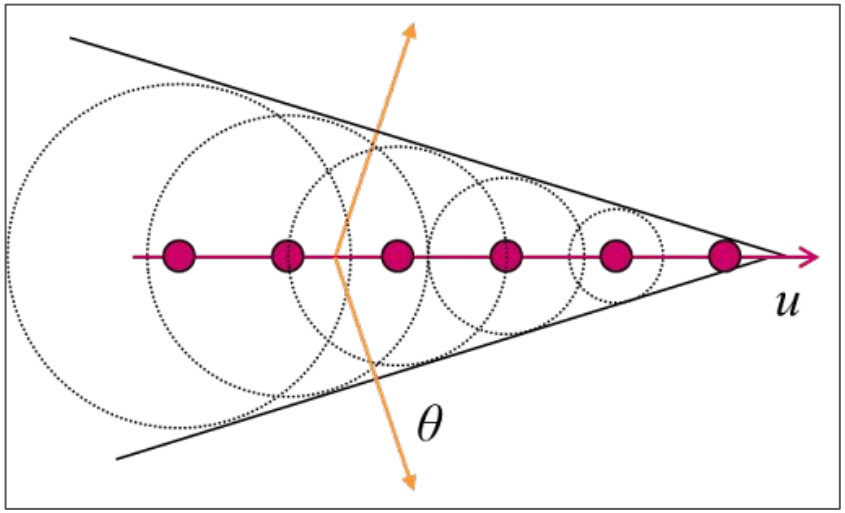
History

Cerenkov Luminescence Imaging (CLI) is a biomedical imaging technique that emerged in 2009, building on the 1934 discovery of Cherenkov radiation by Pavel Cherenkov. Initially used in high-energy physics, CLI applies this phenomenon to medical research by capturing the weak, blue light produced by clinical radionuclides in the body. Key milestones include the 2009 rediscovery of the phenomenon for preclinical research and the first human clinical imaging in 2013, utilizing sensitive optical camera sensors. Advances in instrumentation and multimodal imaging integration have expanded CLI's applications in both preclinical and clinical cancer research, offering a cost-effective, rapid, and multimodal alternative or complement to traditional nuclear imaging methods.

Use of CLI

- **Preclinical research** – low-cost tracer evaluation, biodistribution, therapy monitoring in small animals
- **Radiotherapy monitoring** – visualization of β^- emitters (e.g., 90Y) to confirm dose delivery
- **Surgical guidance** – intraoperative imaging to detect residual tumor tissue or confirm tracer uptake
- **Clinical applications** – feasibility studies in superficial organs (e.g., thyroid with I-131)
- **Hybrid imaging** – combined with fluorescence/bioluminescence for multimodal analysis

a diagram illustrating Cherenkov radiation



a series of concentric circles representing the wavefronts of light emitted by the particle as it moves through the medium.

In tissue, this light is strongly scattered and absorbed, favoring the red to near-infrared wavelengths where Cherenkov output is weakest.

1. Absorption:
    - Haemoglobin, melanin and water in tissue absorb strongly in blue and green wavelengths, but much less in red and near-infrared range (around 650-900 nm)
    - Basically, blue photons are mostly absorbed before they can escape tissue
2. Scattering
    - Shorter wavelengths scatter more strongly in tissue
    - Blue light is scattered multiple times, diffusing and attenuating the signal, while red and near infrared light scatters less and can travel farther to reach the detector

Instrumentation involved in CLI

1. Radiotracer Administration

2. Cherenkov Light Generation

3. Photon Collection (Optical System)

4. Image Acquisition and Processing

5. Display / Surgical Guidance

How does Cherenkov Luminescence Imaging work?

1. Patient Preparation

2. Cherenkov Light Generation in Tissue

3. Photon Detection

4. Image Processing and Co-Registration

Cherenkov light generation

As the radionuclide decays, it emits charged particles that move faster than light in tissue, producing Cherenkov radiation

The intensity and spectral distribution of this light is described by the Frank-Tamm formula, which predicts how many photons are emitted per unit path length and per wavelength interval

Frank-Tamm Formula

The Frank-Tamm formula mathematically describes the number of photons produced by Cherenkov radiation when a charged particle moves faster than light in a medium

$$\frac{d^2N}{dx\,d\lambda} = \frac{2\pi\alpha}{\lambda^2}\left(1 - \frac{1}{\beta^2 n^2(\lambda)}\right)$$

Where:

- $\frac{d^2N}{dx\,d\lambda}$ = number of photons emitted per unit path length (dx) and per unit wavelength interval ($d\lambda$)
- α = fine structure constant (~1/137)
- λ = photon wavelength
- $\beta = v/c$ = particle velocity relative to the speed of light
- $n(\lambda)$ = refractive index of the medium (e.g., biological tissue)

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The amount of radiation needed for CLI?

No fixed amount.

Instead, it depends on several factors.

1. Particle and energy type
2. Properties of the medium
3. Isotope activity
4. Photon yield
5. Depth of tracer in tissue
6. Camera sensitivity and acquisition time

Advantages and disadvantages of CLI

Advantages:

- Cost-effectiveness
- Accessibility
- Unique isotope coverage
- Real-time potential
- Hybrid imaging compatibility

Advantages and disadvantages of CLI

Disadvantages:

- Low light yield
- Limited tissue penetration
- Quantitative challenges
- Background interference
- Not yet widespread clinically

Taken together, CLI represents a novel and versatile approach for visualizing the distribution of diagnostic and therapeutic isotopes in vivo, bridging the gap between optical and nuclear medicine imaging.

Future of CLI

- Clinical translation
- Improved sensitivity
- Hybrid modalities
- Theranostics
- Surgical applications
- New isotopes
- Quantitative imaging

references

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