Cherenkov imaging in the potential roles of radiotherapy QA and delivery

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Abstract. Cherenkov emission has a direct proportionality to the deposited dose at the local level, and capture of these emitted light signals allows visualization of real time maps of dose in vivo. Mapping the Cherenkov signals through water tanks illustrates how 3D Cherenkov can be achieved, either as 2D plus time, or 3D in static imaging. Imaging Cherenkov from patients shows how signals can be acquired which map out radiation dose in real time. The signals are affected by several factors, each of which will take some calibration to resolve, yet intrinsically the signal is shown to be a linear reporter of dose delivered. Development of calibration methodologies is ongoing in both research and development work.

1. Introduction

Relatively recently, the discovery of Cherenkov light emission from radionuclides has been exploited to allow optical imaging of PET agents and therapy monitoring, (Fig 1(a)) in small animal work) [1-3]. The emission is dominant in the blue range (Fig 1(b)) and falls off significantly with increasing wavelength, yet most of the light emitted from tissue is highly attenuated in the UV-blue-green, due to hemoglobin absorption, and so most of the detected light is above 600 nm when imaging tissue. The intensity of emission is a strong function of particle energy (Fig 1(c))[4], however, it is relatively constant in the megavoltage energy range used in radiation therapy. Attenuation within tissue is due to scattering as well as high absorption in the UV-blue-green wavelengths, and so the detected Cherenkov light from animals originates from superficial interactions.

Despite the limitations of Cherenkov light (scattering and absorption limit emission to immediately sub-surface regions) it is apparent that every patient undergoing radiation therapy emits detectable Cherenkov light, and this is a signal which directly reports on the radiation dose delivery. It reports on the combination of patient position, and surface dose delivered. Examples of human imaging of Cherenkov are shown below in Figure 2. Thus, the signal is freely available, and provides potential video coverage of treatment.
Figure 1. The use of Cherenkov light to image $\gamma^+$ or $\gamma^-$ emission is illustrated, as exploited recently to allow optical imaging of nuclear medicine agents. The emission spectrum (b) is dominated by UV-blue light, falling off with a $\lambda^{-2}$ dependence. Emission intensity versus $\gamma^-$ energy (c) increases dramatically in 0.2-2 MeV and then saturates above 20 MeV[5]. Emission yield in radiotherapy >10X higher than PET Cherenkov.

Figure 2. Imaging of Cherenkov emission is shown from a camera beside the LINAC for total skin irradiation (a) and off on the adjacent wall (b) for breast irradiation imaging. Cherenkov images (false color) are shown from total skin irradiation electron therapy (c). The total skin treatment was delivered and imaged using all 6 positions in the Stanford technique (Andreozzi et al, Med Phys 2016), and breast imaging, (d) was shown for both entrance (top) and exit dose (bottom) (Zhang et al, Med Phys 2015). One example of Head and neck treatment beam imaging is shown in (f).

2. Methods
Imaging of Cherenkov emission has been accomplished originally with an ICCD camera (Princeton Instruments, PI-MAX4)[6] mounted on a tripod in the treatment room. This camera is synchronized to the LINAC output current pulse from the target, $I_{\text{Targ}}$, to capture intensified images only during the 3.5 microsecond pulses of the device. The intensifier has a short gate with nanosecond time resolution, allowing the on/off with sufficient temporal resolution to capture the signal only during the pulse on. The pulses are integrated on the CCD camera for approximately 20-40 shots, and then read out as a single image. The LINAC pulses at 360 Hz, and the frame rate from the camera has been 6-20 frames/second. Cherenkov intensity from both water and tissue is strong in this acquisition procedure, with average lateral irradiance approximately several mW/cm². This is also near the irradiance of background room lights as well, so an acquisition of background light without the Cherenkov must be captured, and the two subtracted to yield the contribution of just the Cherenkov. This process works well because they are similar intensities and one does not dominate over the other. Further reductions in background can be achieved through careful choice of the lights used in the room or subdued lighting.

Water-beam imaging has been accomplished with a standard ionization chamber calibration water tank, with the back and side walls painted black, or with black cloth taped to them. A mixture of tap water and 1 g/L of quinine sulphate is used in the tank for a fluorescent reporter of the Cherenkov signal [7-9]. This quinine is there to diminish the acute angular direction at which photons are emitted when charged particle radiation is traveling directly from the beam. Much of the Cherenkov intensity is
directly downwards at a 41° angular cone around the direction of travel of the incident photons and electrons. Secondary scatter blurs this cone a bit, but it is still quite present. This quinine absorbs the UV Cherenkov photons and re-emits them in an isotropic spatial pattern, increasing the laterally directed signal from the beam. Imaging of the beam depth dose 2D profile was examined as was the temporal imaging of the beam in a treatment plan from IMRT and VMAT.

Images on tissue or tissue phantoms are available from Cherenkov emission at either entrance or exit beam. For total skin electron therapy, the camera was positioned beside the linac output (Fig 2(a)), and for breast imaging, the camera was positioned at the side wall, lateral to the patient couch (Fig 2(b)), and just inferior to the beam plane, to avoid penumbra from a lateral beam being incident upon the camera. A 50 mm focal length lens was used with f/1.8 aperture. The processed image of one patient from each of total skin treatment (c) and whole breast irradiation (d) are shown in Fig 2. In the case of the total skin, there were 6 poses for each patient and images of each pose are shown. In the case of total breast irradiation with 6 MV photons, the entrance beam dose (top) and the exit beam dose (bottom) could be captured independently on one side of the patient.

Figure 3. The LINAC beam geometry used experimentally is shown (a), with simulation geometry (b). Experimental images of beam at angles 0°, 15°, 30° and 45° (c) around the square beam. [8, 12]

3. Results

3.1 Water Tank Imaging

The collisional energy loss of secondary electrons leads to dose in tissue, and the soft-collision radiative energy loss due to Cherenkov emission are independent processes, but both are largely energy independent above 220 keV. This proportionality in energy loss per unit path length at the majority of the electron energy spectrum used in clinical radiotherapy is the fundamental basis for use of Cherenkov emission imaging as a dosimetry surrogate. Despite disproportionality at energies less than 220 keV, the range of these low energy electrons is less than 1 mm. The dose distribution is largely dictated by energetic electrons above the threshold value for Cherenkov emission. Indeed this is well known, as Monte Carlo simulations of dose often do not track secondary photons <200 keV because they contribute so little to the overall dose[4]. A Dose/Cherenkov comparison has been systematically examined in water, using the geometry of Figure 3, and showing measured data from depth dose and profile curves in Figure 4.
While Cherenkov light is emitted at exactly 41° from the direction of travel of the electrons, we have found that by adding fluorescent dye quinine sulphate (used in tonic water) to water tank experiments, we could then image the fluorescent light which was generated by Cherenkov excitation of the dye, and this fluorescent emission is isotropic [7, 11]. Images of emission from the water tank are shown in Figure 6. In Figure 7, we demonstrate the ability to use these lateral profiles at multiple angles to reconstruct a 3D map of Cherenkov emission, which is a direct surrogate for 3D dose. We have recently demonstrated the ability to verify IMRT and VMAT treatment plans in water tanks [8], and also for imaging of large area complex beams in water tanks [8, 12].

The images and data in this water imaging clearly indicate there is an outstanding match between the observed Cherenkov fluorescence and the deposited dose in water. Monte Carlo simulations indicated Cherenkov-fluorescence to dose has linear proportionality and that the agreement was better than 5% accuracy in complete IMRT and VMAT treatment plans [8].

3.2 Patient imaging – delivery verification

Human pilot studies were completed comparing Cherenkov intensities on the patient to predicted doses from the treatment planning system and to thermoluminescent diode (TLD) measurements on the same patients. Some preliminary data taken from patients illustrate that, on a case study, there is good linearity between dose per field planned and Cherenkov intensity recorded experimentally. In this case, shown in Figure 5, the doses for a collection of subjects at the 6 MV entrance field match the planned fraction dose very well with a linear regression between the two. The match between these data is still under investigation, with comparisons being studied on exit doses and 10 MV doses, for those subjects given the split dose regime. The data in Figure 5(c) clearly shows a linear dependence of Cherenkov intensity with dose. The figure shows correlation exists between planned skin dose and Cherenkov imaged dose for 10MV tangent beams. Other calibration factors are likely needed in some circumstances, such as pigmentation, incident angles, energy level and exit vs. entrance dose to correct for Cherenkov emissions compared to delivered dose. A full validation of these factors in phantom work has been tested and calibration factors determined [13],

![Figure 4](attachment:image.png)
Figure 5. Visualization of surface dose (5mm depth) in a treatment plan is shown in (a) and the Cerenkov image captured during the patient’s treatment is shown in (b). Maps of dose (cGy) per fraction versus imaged Cerenkov intensity were used from 6 subjects to create a linear calibration line (c). This type of imaging could allow real-time detection of delivery and verification of delivered dose, at video rate.

4. Discussion
Cherenkov video imaging is early in the development process, but it has the potential to pave the way for a number of innovations in radiation therapy imaging, such as in the areas of quality audit, and treatment verification. Applications of in vivo imaging to date have largely focused on whole breast irradiation because of the match to large soft tissue surfaces which need verification. However less used applications such as total skin irradiation are also good applications of this methodology, because of the need for large complex surface area dosimetry, in a setting where few tools exist to capture the signal.

The most immediate proposed development areas from this work include:

1) The demonstration that radiation dose delivery could be visualized, naturally in real time, implicitly verifying what is happening. This has both scientific and real life implications.

2) Direct ability to monitor beam shape in real-time on the patient’s skin throughout the treatment by the radiation therapy team in comparison to that predicted by the planning system, tracking treatment fields with dynamic multi-leaf collimator movement. Cherenkov images can be superimposed on the normal video stream that the radiation therapists typically view. Our experience to date suggests that it increases the radiation team’s comfort in knowing the plan is being delivered as intended, by directly viewing it throughout the duration of each treatment.

3) The treatment can be recorded for permanent archive to determine what happened in the cases of complex treatment QA audits.

4) The high sensitivity to blood vessel location provides internal patient soft tissue anatomy, which could be used for highly accurate treatment verification and positioning to an accuracy of 1mm. These internal biologic “fiducials” can indicate inaccurate alignment or when fiducials are distorted in combination with change in measured exit could indicate anatomy changes and need to re-plan the patient’s treatment.

5) The Cherenkov intensity is generally proportional to dose, so the images could be interpreted as surface dose maps, once more fully calibrated as proposed here.

These are innovative roles for Cherenkov imaging, and will be tested in future research and development of the methods for image capture and calibration. Ongoing work in calibration is perhaps the most important part of determining the role for Cherenkov imaging in radiotherapy.
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6. References
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