BEAM INDUCED FLUORESCENCE EXPERIMENTS FOR ULTRA-HIGH-DOSE-RATE DOSIMETRY IN PROTON THERAPY

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Abstract

Ultra-High-Dose-Rate (UHDR) / FLASH radiotherapy with proton pencil beams requires particle fluxes that saturate current clinical dosimeters. Before UHDR proton therapy can be clinically implemented, novel dosimetry techniques must be developed that reduce the uncertainty in the delivered dose to clinically acceptable levels. One promising solution is to image gas Beam Induced Fluorescence (BIF), where the photon yield and transverse profile can be combined to calculate an absolute dose.

Using the AGOR cyclotron at the Particle Therapy Research Center, a superconducting isochronous cyclotron capable of providing proton beams at clinical energies and dose-rates well into the UHDR regime, we are assessing the feasibility of using BIF for dosimetry. We show that the photon yield of nitrogen remains linear with dose even with UHDR pencil beams and examine the gas pressure-dependence in the range from 10^{-3} to 100 mbar. The width of the fluorescence region is compared to the transverse beam size and methods to remove the background neutron and gamma counts from the CCD image without significantly altering the photon yield are discussed.

ULTRA-HIGH DOSE-RATE DOSIMETRY

Dosimetry is essential for radiation therapy beam control and quality assurance. Current dosimetry methods, such as ionisation chambers, solid state detectors or scintillators, are optimised for conventional clinical dose-rates ~ 0.01 Gy s^{-1}, but suffer from recombination, quenching and radiation hardness problems at higher dose-rates [1]. Ultra-High Dose-Rate (UHDR) irradiation has been increasingly studied since the rediscovery of the FLASH effect in 2014 [2] - a normal tissue sparing effect for the same tumour control probability when irradiations occur at average dose-rates > 40 Gy s^{-1}. For hadron therapy, achieving these dose-rates with pencil beam scanning would require instantaneous dose-rates $\sim 10^2$ to 10^4 Gy s^{-1} depending on the beam time-structure, driving the need for UHDR compatible dosimetry.

The main criteria for an active radiotherapy dosimeter are a high linearity with dose independent of the dose-rate and to be minimally invasive to the beam. We present here the results of proof-of-principle tests of an optical dosimetry method based on the detection of gas Beam Induced Fluorescence (BIF) that is optimised for UHDR proton pencil beams and compatible with conventional dose-rates. As BIF occurs already in medical beam lines (with residual gas or in air gaps e.g. before a gantry), it is expected to fit both criteria. BIF is typically used for beam profile monitoring when minimally invasive instrumentation is required, for instance with high power beams, heavy ions, low energy or low beam currents [3–6], but if the light intensity is measured as well, the profile and intensity can be used for absolute, real-time dosimetry.

BEAM INDUCED FLUORESCENCE

BIF is the emission of characteristic photons (scintillation) from gas molecules ionised/excited by the beam of a particle accelerator. The intensity and transverse profile of the observed fluorescence depend on the beam parameters (total number of protons delivered, N_p, energy E), the gas (composition, molecular density ρ, lifetime of excited states, spectral range, cross section σ), the imaging system (quantum and transmission efficiencies ϵ_{det}) and geometrical factors (length of fluorescence L, solid angle acceptance ϵ_{geo}), with the number of photons detected by an optical system,

$$N_\gamma = N_p \, f(\rho) \, \sigma(E) \, L \, \epsilon_{\text{geo}} \, \epsilon_{\text{det}}, \qquad (1)$$

where $f(\rho)$ is a non-linear function that describes the ratio of radiative to collisional de-excitations. It depends heavily on the gas species chosen and the band-pass of the optical system which dictate the transitions that are imaged, as shown by Hampf et al. [7]. For ionised gaseous species, the photon emission saturates with increasing gas density due to collisional quenching and electron-ion recombination; for atomic transitions, the photon emission increases continuously with gas density and can even be super-linear due to secondary electron excitations. For a system with a wide band-pass such as an EMCCD + camera lens, the observed pressure dependence will be a combination of both of these effects.

For a given pressure, the photon emission is a direct measurement of the beam energy loss. Plum et al. [8] measured this energy loss as 3.6 keV per visible photon for nitrogen and, along with the results of Forck et al. [9], the cross-sections, photon yields, fluorescence lifetimes and emission spectra of nitrogen and the Noble gases are well known. We take nitrogen as a specific example and hypothesise that, with its fluorescence lifetime of ~ 60 ns [8] and its stopping power [10] together with Eq. 1, BIF satisfies the main criteria for dosimetry: namely the linearity with delivered dose (total charge) and dose-rate (beam current) independence.

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SETUP AND METHODS

The two most prominent peaks in the BIF spectrum of nitrogen occur at 391.4 and 427.8 nm [8,9]. To image this spectrum we used two high speed EMCCD cameras (Princeton Instruments ProEM-HS:512BX3) with quantum efficiency down to 300 nm paired with two Schneider Optics Varigon 1.8/12.5-75 lenses placed ~ 1 m from the beamline. Shielding of paraffin and lead was placed around the cameras which were focused on two independent blackened internal chambers (coated with Thorlabs BKF12 matte black). The gas pressure was controlled in the range 10^{-3} to 100 mbar in roughly order of magnitude steps with a constant incoming flow of nitrogen and a vacuum pump. Beam current and total delivered charge were measured with a Faraday cup and a retractable wire chamber was used for upstream beam profile measurements, see Fig. 1.

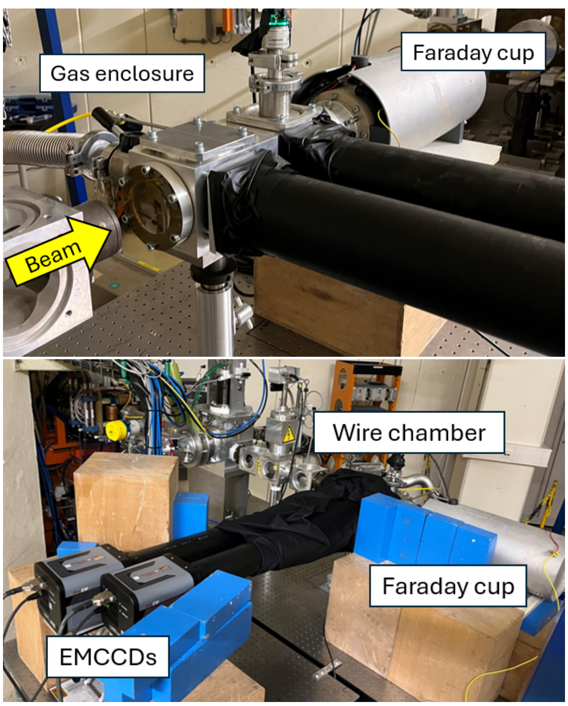

Figure 1: Experimental setup for nitrogen BIF dosimetry proof-of-principle experiment at PARTREC.

All irradiations used a 150 MeV proton beam from the AGOR isochronous cyclotron (bunch frequency 55 MHz) with nominal beam currents of 1, 10, 100 and 1000 nA (~ 10^2 to 10^5 protons per bunch) and Gaussian profile (σ = 1.6 ± 0.1 mm) at the target. For each current, total delivered charges from around 1 to 120 nC were delivered. The Faraday cup was used to measure beam current and delivered charge. However, due to setup limitations, the Faraday cup was not under vacuum, so there is a high systematic error. Since we are investigating a scaling relationship between the camera signal and the delivered charge, not absolute measurements, this was deemed acceptable here.

Images were taken with the EMCCD exposure time set greater than the duration of the beam delivery and the electron multiplier gain was set to 100, found empirically to correspond to an actual gain factor of 60 ± 1. To remove the hot pixels from neutrons and gamma rays incident on the CCD chip, the images were filtered with a 2D standard median filter (SMF). SMF iterates through every pixel of the image and replaces its value with the median of the surrounding k x k pixel grid, where k is the kernel size. At the image edges, the kernel size is automatically adjusted. This is a standard technique for removing salt-and-pepper type noise. For each irradiation, the fluorescence profile and total light yield were calculated from stacked columns of the filtered camera images.

EMCCD IMAGES

An example image is shown in Fig. 2 with the background camera image subtracted. The top image shows the pixel values clipped to a maximum of 4000 ADU. This is done to make the beam fluorescence (with pixel values up to ~ 3500 ADU) visible alongside the hot pixels from neutron and gamma incidences (~ 45000 ADU). The same image is also shown after application of a 2D SMF with kernel size 9 where the hot pixels have been filtered out. The kernel size was chosen by iteratively filtering and checking for remaining hot pixel spikes before increasing the kernel size further until the stacked profiles, see Fig. 3, were smooth. A kernel size of 9 was implemented to all camera images.

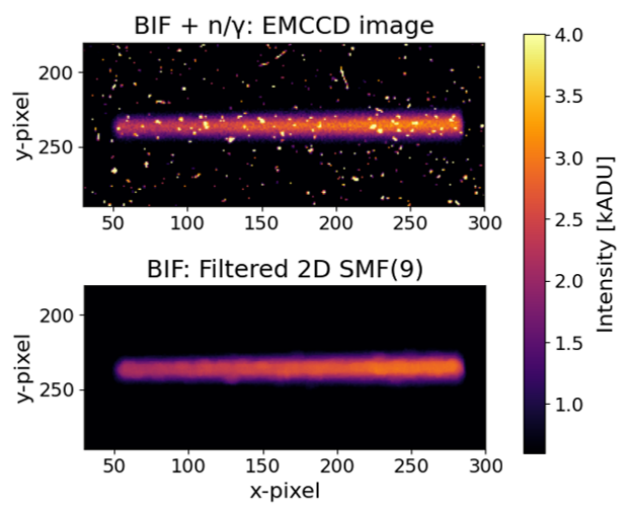

Figure 2: Example EMCCD image of 96 mbar nitrogen BIF from 126 nC delivered at 1005 nA pre (top) and post (bottom) filtering background neutron/gamma counts.

In Fig. 3, the fluorescence profile is compared between the unfiltered and filtered background subtracted image above for a run of 10 pixel columns stacked together. From a Gaussian fit to the filtered profile, σ_{EMCCD} = 6.3 pixels equal to 1.2 mm. This is slightly narrower than the wire chamber measurement just upstream of the gas enclosure which measured σ_{wire} = 1.6 ± 0.1 mm, however the beam focus was in-between the wire chamber and the gas enclosure, so limited comparisons between the transverse beam dimensions and the fluorescence profile width can be made from these results. The fluorescence signal (in ADU) is then computed by integrating the filtered stacked profile.

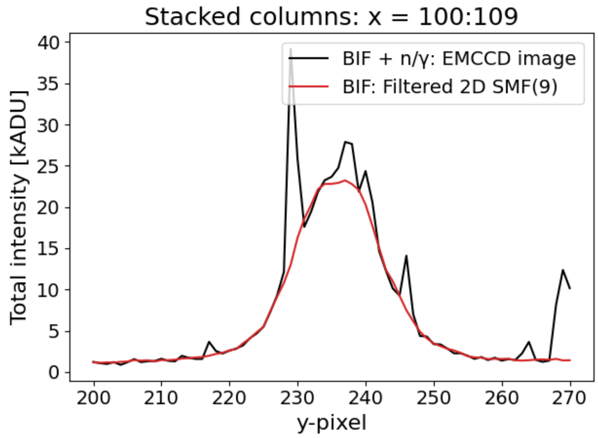

Figure 3: Fluorescence profiles from the example EMCCD image with and without standard median filtering (SMF).

It is noted that the median filtering process causes a flat-top effect around local maxima with length scale ~ half the kernel size. We are currently developing alternative filtering protocols that reduce this effect, but here, since the kernel size is constant and the beam profile and divergence were not changed throughout, this flat-top effect is taken as a systematic uncertainty.

DOSE, DOSE-RATE AND GAS DENSITY

From the beam energy and transverse size, we estimate that each nC of delivered charge corresponds to ~ 2 Gy for water equivalent dose in the Bragg peak region (using [10]). Hence we take the charge as a proxy for dose and, accordingly, the beam current as a proxy for average dose-rate, giving us a range from ~ $2-200$ Gy delivered at ~ $2-2000$ Gy s^{-1}. Time resolution at the scale of the isochronous cyclotron bunches (55 MHz RF) was not achievable with our EMCCD system, hence only integrated values are quoted, and systematic errors in camera "signal" and charge measurements are present, as mentioned above, but not computed, since we are primarily interested in the scaling between these parameters, not absolute values. Full error propagation is deferred to future publications.

The first requirement for dosimetry is demonstrated in Fig. 4. From Eq. 1, it is expected that the signal scales linearly with the delivered charge, Q, or equivalently, dose. The total fluorescence signal (from the integrated filtered stacked columns, e.g. Fig. 3) is plotted against Q for nominal beam currents of 1000 nA and 0.7 nA (between each irradiation the actual beam currents fluctuated by ~ 10%) showing near perfect linearity, $R^2 > 0.999$, and gradients within 0.1% for both beam currents.

Figure 5 shows the dependence of the fluorescence signal on the gas pressure (proxy for density) from 10^{-3} to 100 mbar. Pressures were increased in order of magnitude steps and a charge scaling graph like the one in Fig. 4 was produced for each. The gradients of these graphs, "signal/Q",

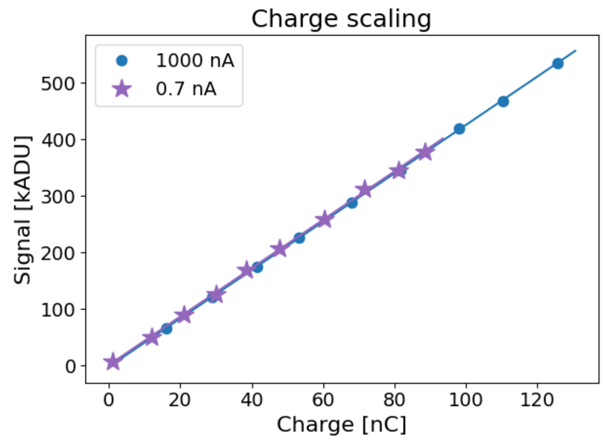

Figure 4: Dose linearity and dose-rate independence of the integrated filtered fluorescence profile. Uncertainties are not fully computed at this stage, see main text.

follow the expected qualitative description of $f(\rho)$ given above with a combination of ionic transitions saturating and neutral molecule transitions increasing with gas density. A fit to the data is deferred to future publications. Again, this scaling is dose-rate (beam current) independent.

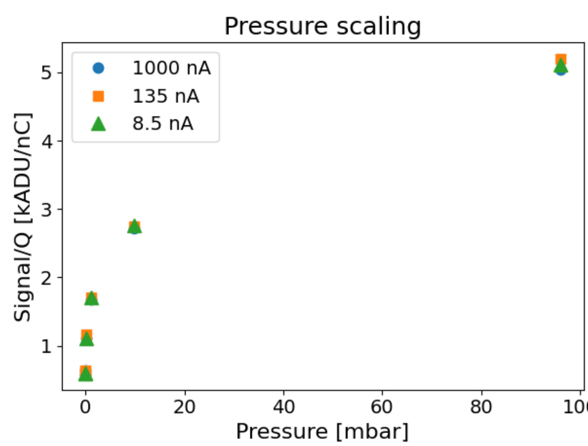

Figure 5: Dose-rate independent pressure scaling of the integrated filtered fluorescence profile. Uncertainties are not fully computed at this stage, see main text.

CONCLUSIONS

An EMCCD camera used to image nitrogen Beam Induced Fluorescence of a 150 MeV proton beam from the isochronous AGOR cyclotron (55 MHz RF) has been shown to meet the two main criteria for absolute dosimetry, namely signal-dose linearity and dose-rate independence, for doses from ~ $2-200$ Gy and average dose-rates ~ $2-2000$ Gy/s. Although only scaling relationships were measured here (not absolute dose, charge etc), the results suggest that BIF imaging is a viable method for UHDR dosimetry with proton pencil beams. Further work with better control of systematic uncertainties, such as EMCCD image filtering, and with actual dose measurement is however, still necessary.

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