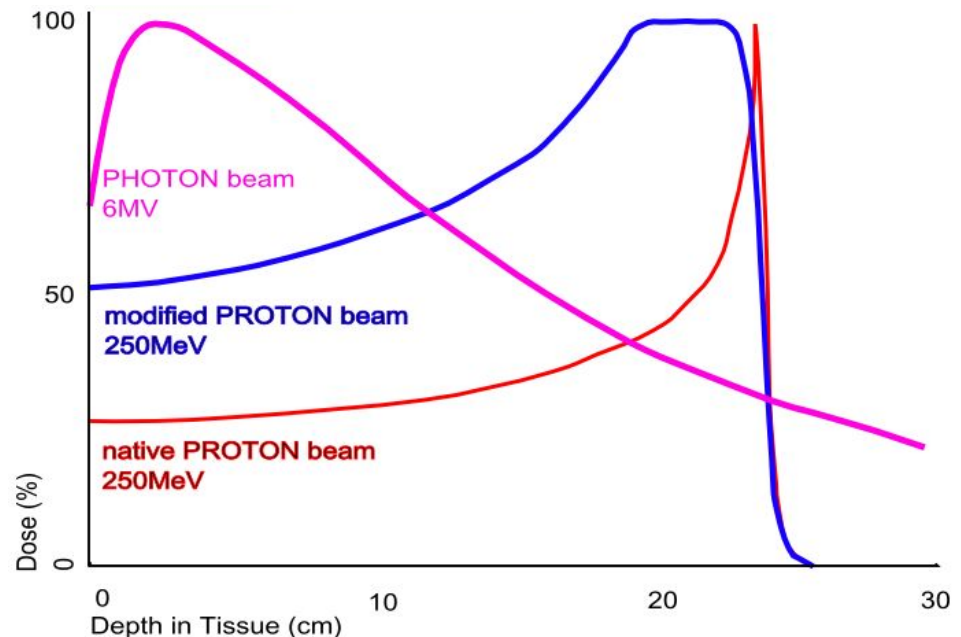


Calorimetry for Cancer Proton Therapy – Can We Help?

Anastasia Basharina-Freshville
(University College London)

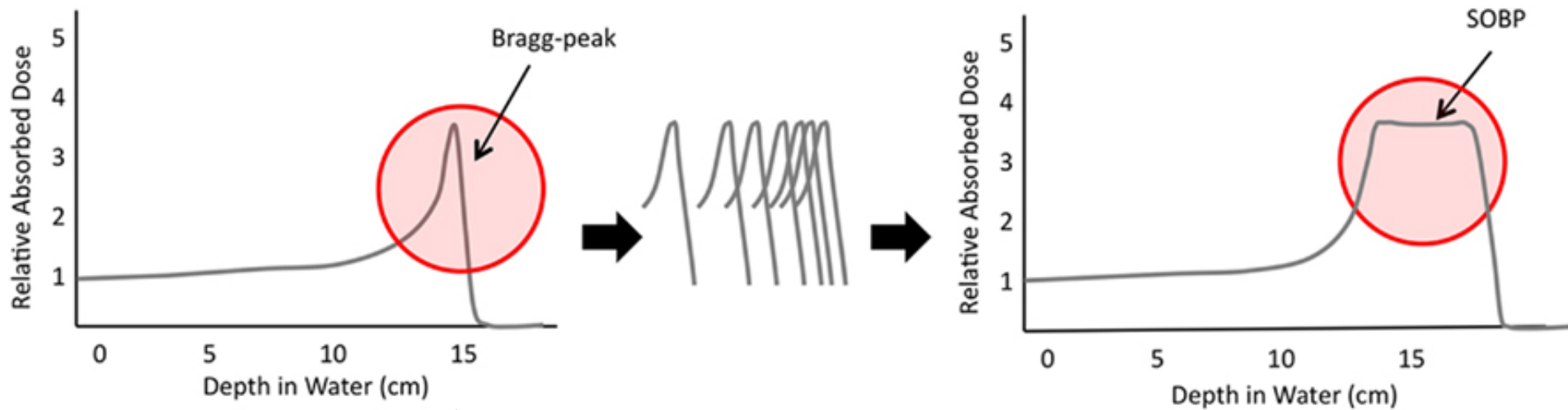
Why Proton Therapy?

- More precise form of radiotherapy
- Precise tuning of the delivered dose to the patient through careful selection of proton beam energy
 - Due to energy loss profile of protons
 - And much smaller beam spot sizes
- Important for areas where we particularly want to avoid large doses of radiation to healthy tissue:
 - Head and neck
 - Central nervous system
 - In children



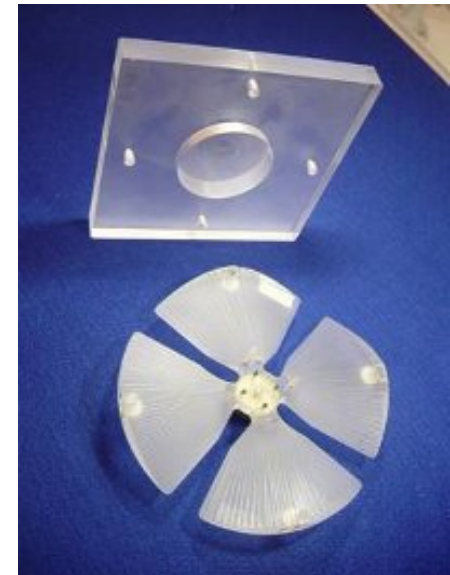
<http://samhs.org.au/Virtual%20Museum/xrays/Braggs-peak-rxth/braggpeakrxth.htm>

Why Proton Therapy?



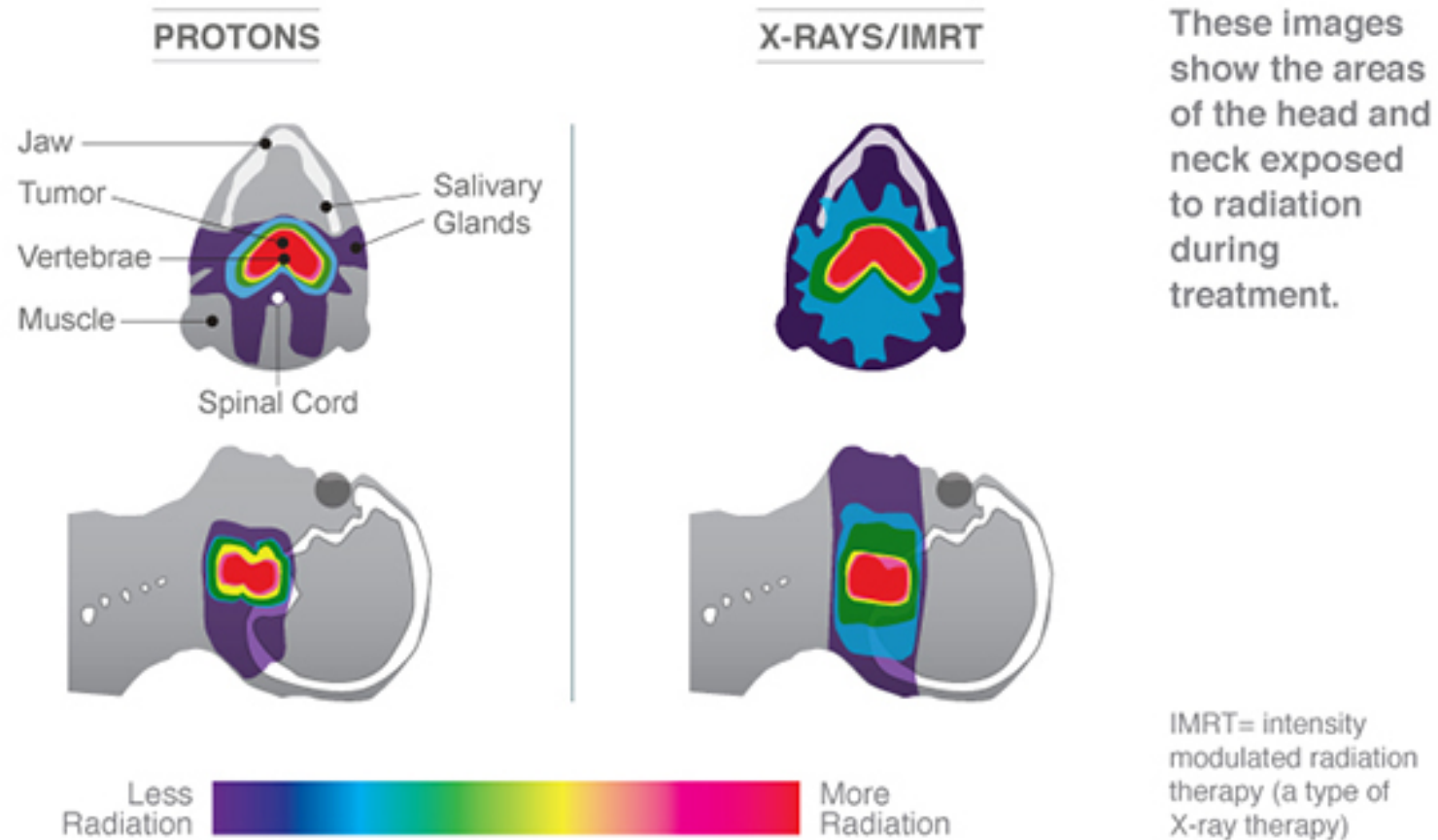
Front. Oncol., 06 September 2011 | doi: 10.3389/fonc.2011.00024

- Range shifter and modulator used for a **S**pread **O**ut **B**ragg **P**eak
- Alters beam energy to provide a uniform dose over the depth of the tumor



<http://www.clatterbridgecc.nhs.uk/professionals/physicsdepartment/cyclotron/>

Base-of-Skull Tumors: Proton therapy delivers less radiation to nearby healthy organs than X-rays¹⁰



<http://www.seattlecca.org/diseases/proton-therapy-head-neck-cancers.cfm>

Proton Therapy Challenges

- Precise measurements of **beam energy** and **energy spread**

- Target: **~1% level**

Our starting point!

- **Proton imaging**

- Requires an **increase in imaging resolution** compared to X-ray based systems due to localisation of proton dose delivery
- Currently use a **conversion factor** to convert from X-Ray based imaging systems to proton therapy treatment plans, which introduces **imprecision**
- Currently, the **patient** is **imaged away** from the **treatment** – any movement of the patient's anatomy introduces further **imprecision**

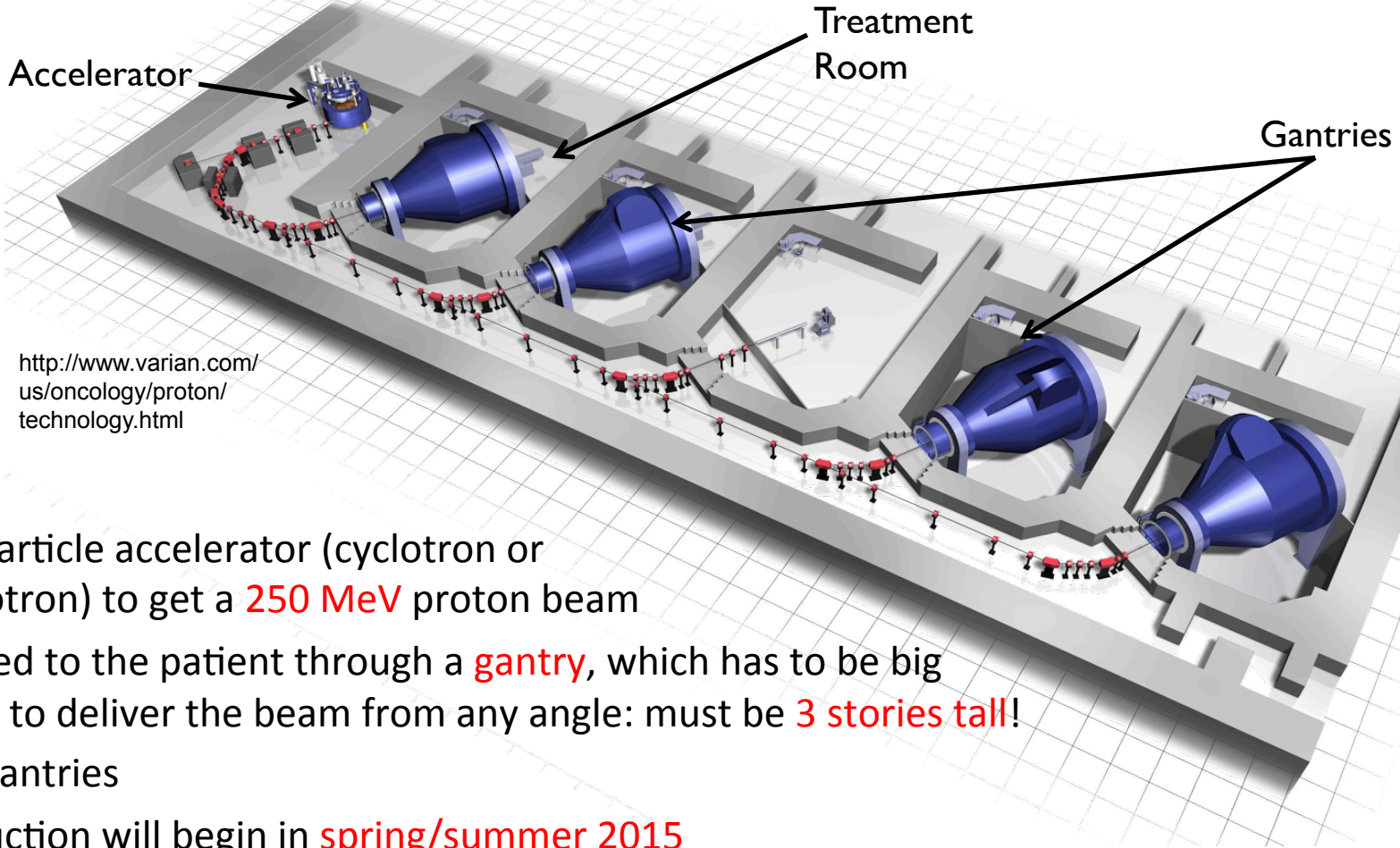
- **Neutron background**

- Neutron background flux at proton therapy facilities is **poorly known**
- Must be measured to **avoid adverse biological effects** to the patient

Proposed Solutions

- Calorimetry approach for beam energy and spread measurements
 - ↑
The focus of this seminar
- Proton imaging:
 - Image with > 300 MeV proton beam, which will emerge from the body without significant energy deposition
 - Tomography approach:
 - A series of tracking layers upstream and downstream of the patient
 - Accurate calorimeter for energy measurements
 - Target: ~0.5 – 1% for 300 MeV imaging protons
- Neutron background:
 - Calorimetry approach (discussed in “Future Plans”)

UCLH Proton Therapy Centre

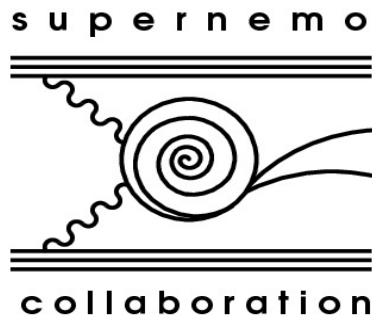


<http://www.varian.com/us/oncology/proton/technology.html>

- Use a particle accelerator (cyclotron or synchrotron) to get a **250 MeV** proton beam
- Delivered to the patient through a **gantry**, which has to be big enough to deliver the beam from any angle: must be **3 stories tall!**
- Three gantries
- Construction will begin in **spring/summer 2015**
- First patient treatment: three years from start of construction

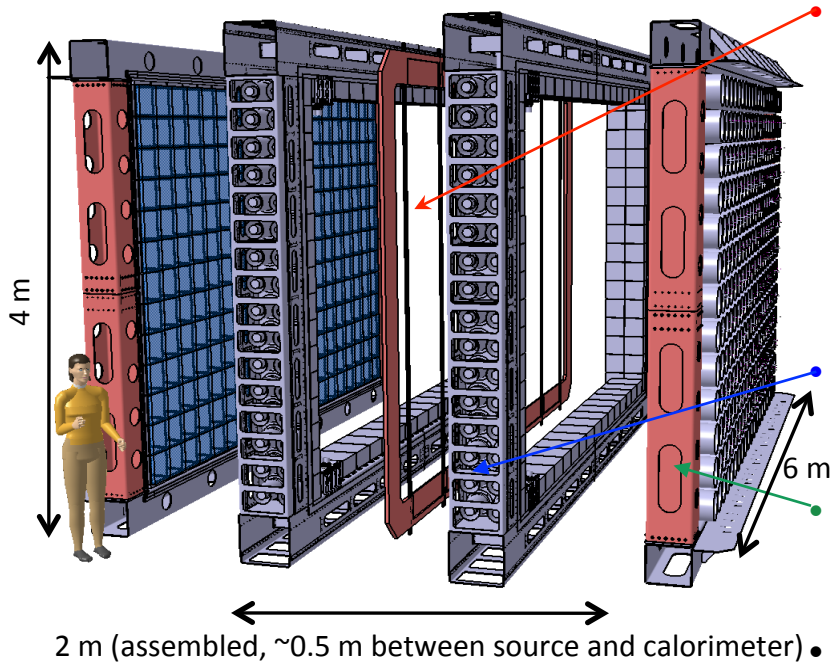
↑
Can we work on some of the challenges before then?

SuperNEMO



- **Neutrinoless double beta decay** detector using NEMO3's **tracker-calorimeter** technique
Target sensitivity: $T_{1/2} > 10^{26}$ years $\rightarrow \langle m_{\nu} \rangle < 0.04 - 0.1$ eV
- **Modular** detector with a planar geometry

1 module (of 20) consists of:



Source foil:

- 5 kg (total of 100 kg) of 40 mg/cm² (4 x 2.7 m²)
- ⁸²Se (high $Q_{\beta\beta}$, long $T_{1/2}^{2\nu\beta\beta}$, proven enrichment technology): starting baseline
- ¹⁵⁰Nd and ⁴⁸Ca being considered depending on enrichment possibilities

Tracker: ~2000 drift cells in Geiger mode

\rightarrow particle identification (for background suppression)

Calorimeter: ~550 scintillator blocks + PMTs

\rightarrow energy and time of flight measurements of particles

Passive shielding surrounding each module

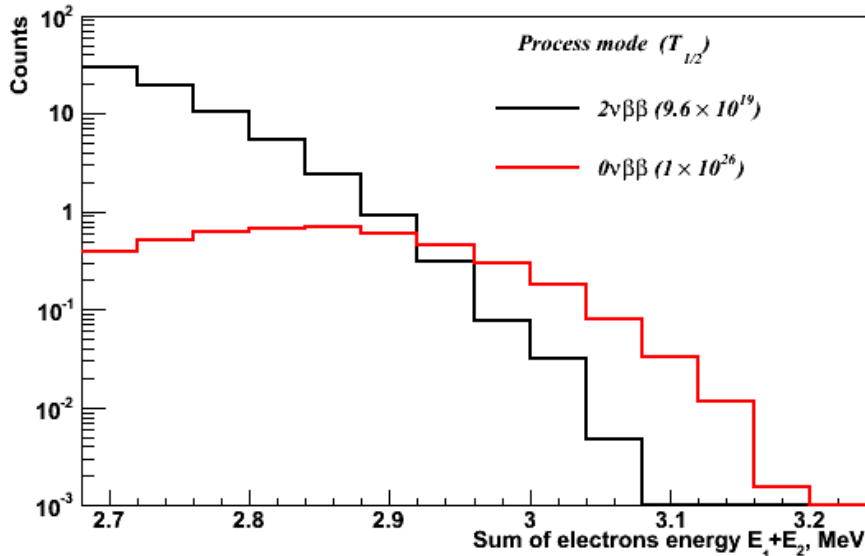
From NEMO3 to SuperNEMO

- Energy resolution is one of the main challenges (factor of 2 improvement):

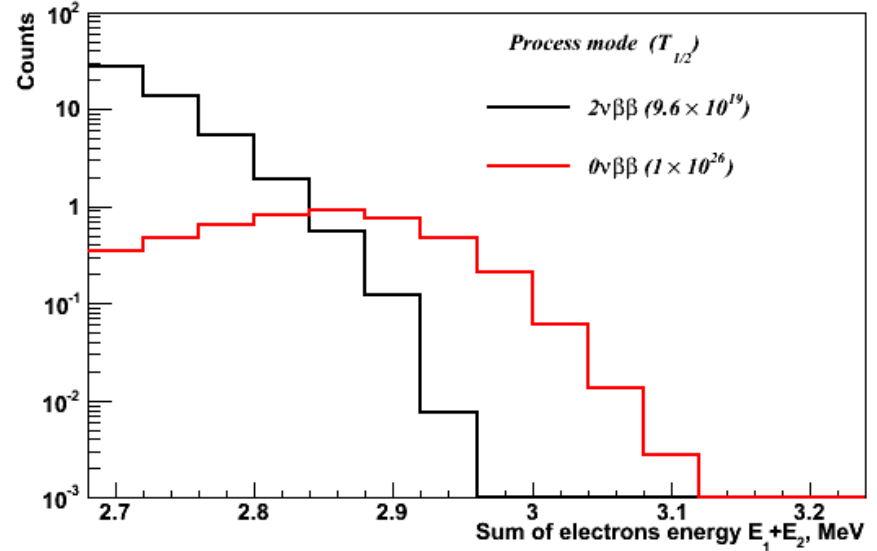
$$\begin{array}{ccc} \text{NEMO3:} & \longrightarrow & \text{SuperNEMO:} \\ \frac{14-17\%}{\sqrt{E}(\text{MeV})} & & \frac{7\%}{\sqrt{E}(\text{MeV})} \end{array}$$

- SuperNEMO scintillator has to be **organic plastic scintillator** (high light yield, low electron back-scattering, high radiopurity, fast timing)
 → Can 7% FWHM at 1 MeV be reached for organic solid plastic scintillator?
- First step in SuperNEMO R&D: secured STFC funding for energy resolution R&D

SuperNEMO demonstrator: 500 kg × y of ⁸²Se, FWHM 12% @ 1 MeV



SuperNEMO demonstrator: 500 kg × y of ⁸²Se, FWHM 7% @ 1 MeV



Energy Resolution

$$\frac{\Delta E}{E} = \frac{2.35\sigma}{E} = \frac{2.35}{\sqrt{N_{pe}}}$$



Three experimental objectives:

$$\left(\frac{N_{ph}}{E_e}\right) \cdot \epsilon_{col}^{light} \cdot (QE^{PMT} \cdot \epsilon_{col}^{PMT}) = N_{pe}$$

scintillator light output

Physically translates to:

- **Scintillator**: material, surface treatment, geometry
- **Reflector**: material, reflectivity coefficient, specular/diffusive
- **Optical coupling quality**: material, geometry, light guides
- **Photomultiplier Tubes (PMTs)**: quantum efficiency (QE), collection efficiency, gain of the first dynode

Combined in an “**optical module**”:

scintillator wrapped in reflective material coupled to a PMT

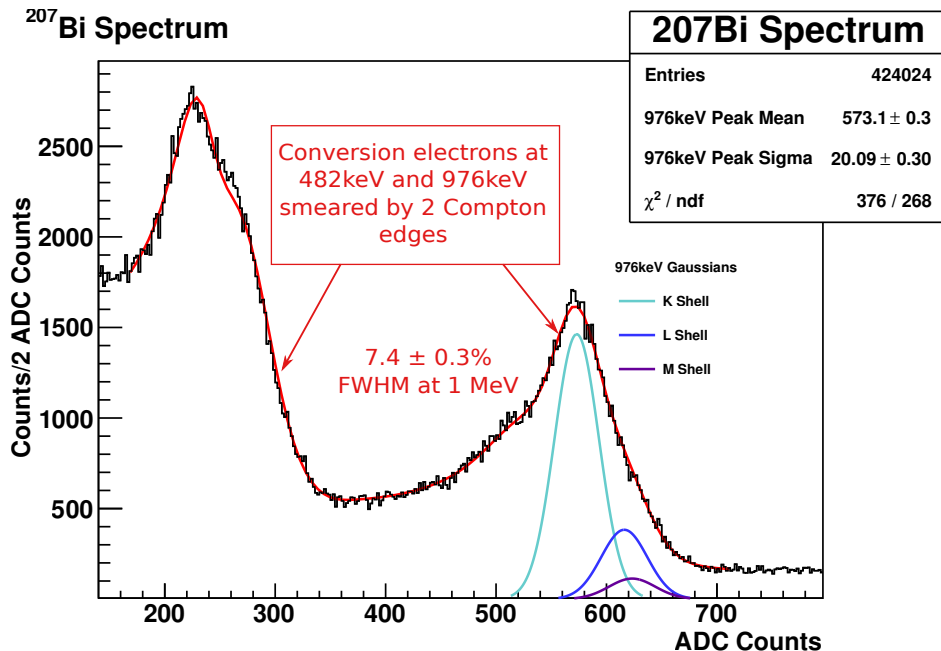
σ	sigma of distribution
E	mean of distribution
N_{pe}	number of photo-electrons
N_{ph}/E_e	number of photons per unit energy
ϵ_{col}^{light}	light collection efficiency
QE^{PMT}	quantum efficiency of the photo-cathode
ϵ_{col}^{PMT}	PMT collection efficiency

SuperNEMO Calorimeter Test Bench

Excite scintillator with a **monochromatic electron source** (approximates the delta function)
 → any **smearing** of distribution is due to **detector properties**

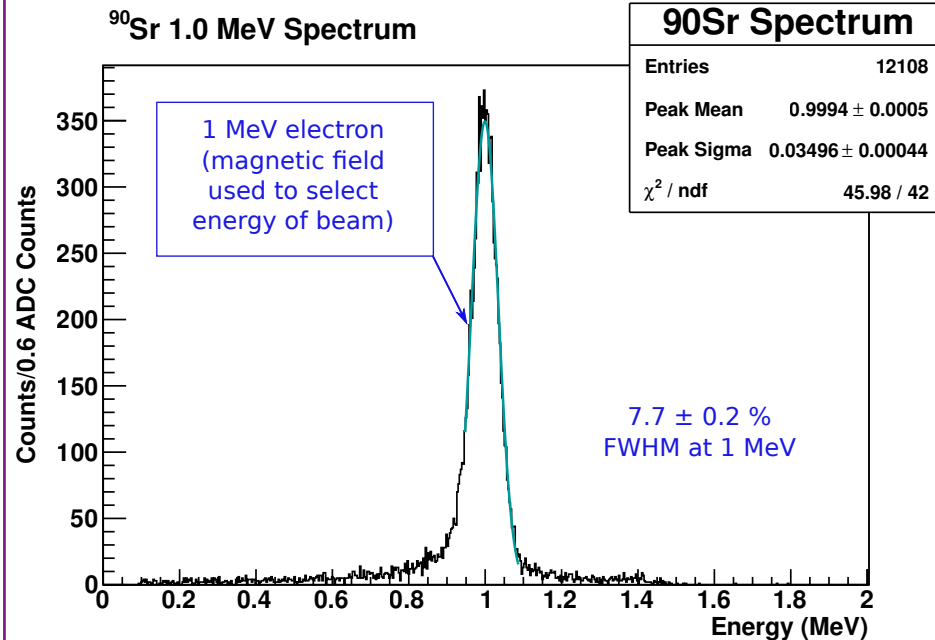
UCL:

- **²⁰⁷Bi source:** 976 keV and 482 keV K-shell conversion electrons
- **Fit:** deconvolution of X-rays, γ s, L-shell and M-shell conversion electrons



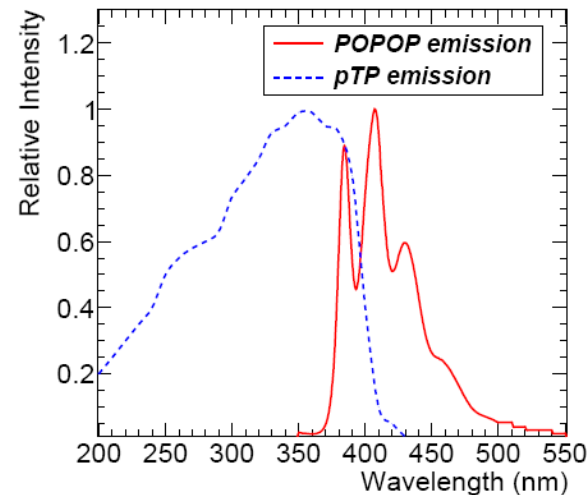
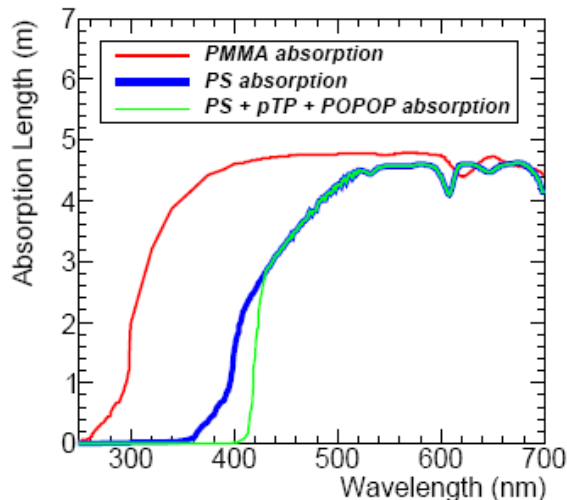
Bordeaux:

- **⁹⁰Sr spectrometer:** ⁹⁰Sr beam passed through a magnetic field to select monochromatic electrons of known energy
- **Fit:** Gaussian



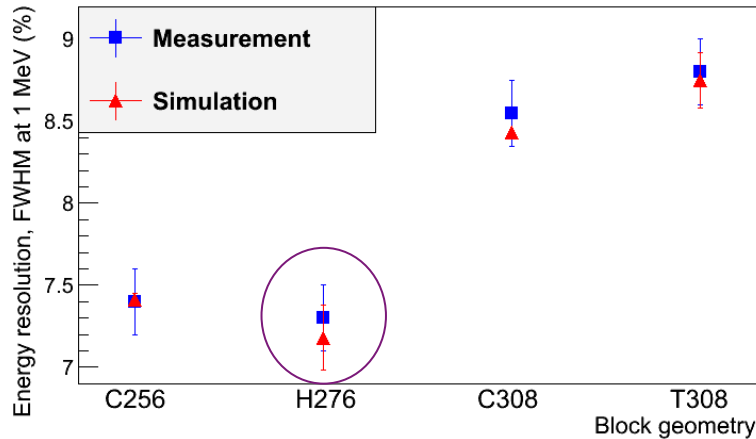
SuperNEMO Calorimeter R&D: Simulations

- Full **calorimeter** simulations:
 - GENBB event generator
 - Physics simulations with GEANT4 (optical photon transport in scintillator detectors)
- The model accounts for **wavelength dependence** of optical properties, all of which have been **experimentally measured**, of the:
 - scintillators (self absorption and re-emission)
 - reflective wrappings
 - photomultipliers (QE)
 - optical coupling materials
 - refractive index of optical materials



SuperNEMO Calorimeter R&D: Scintillators

- Block **shape** studies:



C256: cubic 256² x 190 mm²
H276: hexagonal 276 mm diameter with 12 mm minimum depth
C308: cubic 308² x 190mm²
T308: cubic 308² x 190mm² with tapered sides

- Material:** polystyrene (PST) vs. polyvinyl toluene (PVT)

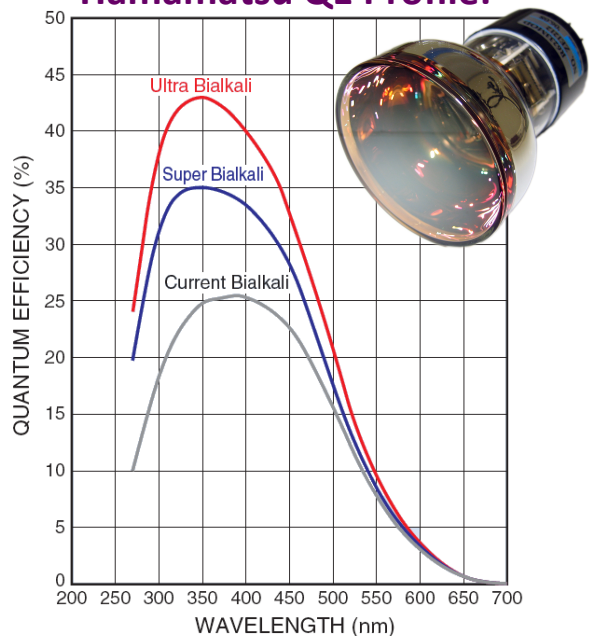
Material	$\frac{\Delta E}{E}$ (%)	f_{FWHM}
NEMO-3 PST	8.9 ± 0.2	1.
EJ-200 PVT	8.3 ± 0.2	1.07 ± 0.03
EJ-204 PVT	7.8 ± 0.2	1.12 ± 0.03

- Close collaboration with manufacturers (JINR Dubna, ISM Kharkiv, ENVINET, ELJEN) for contents of:
 - PPO scintillating agent
 - POPOP wavelength shifter
- Surface finishing:** polished vs. depolished
 - All surfaces depolished (machine finish), with the face with the hemispherical cutout polished

SuperNEMO Calorimeter R&D: PMTs

Photocathode QE:

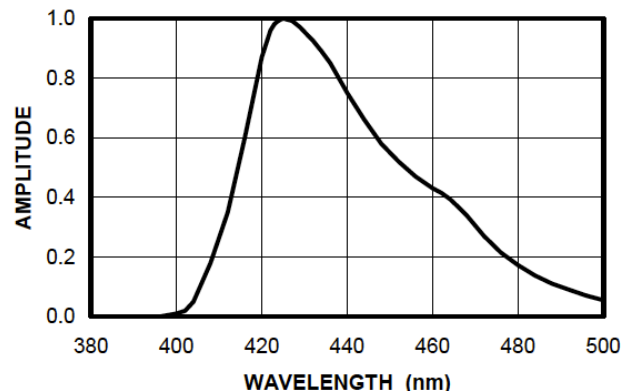
Hamamatsu QE Profile:



- Bi-alkali alloy development for photocathode material has achieved $QE > 40\%$

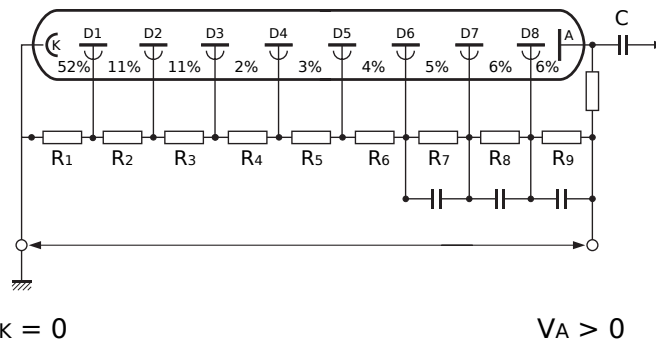
- Close collaboration with Hamamatsu to optimise QE to the emission spectra of the scintillator

EJ-200 EMISSION SPECTRUM



Collection efficiency (close collaboration with Hamamatsu on 8" R5912-MOD tube):

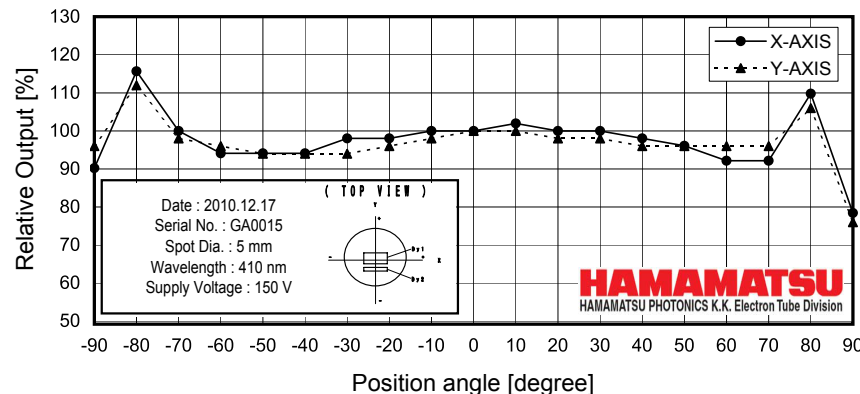
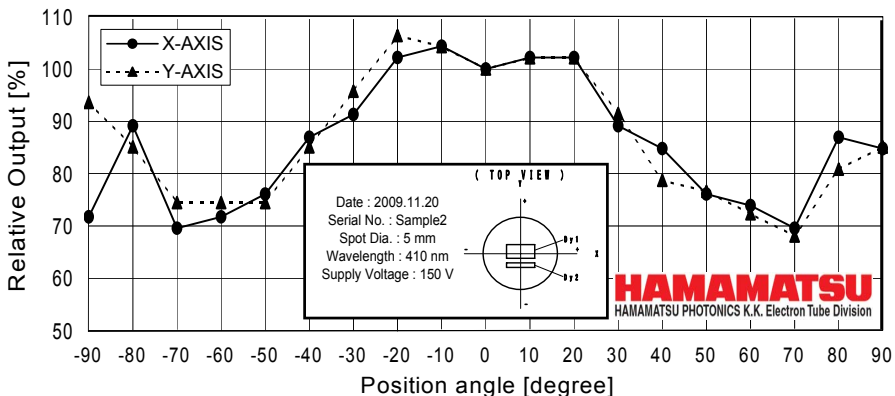
- Number of dynode stages reduced from 10 to 8
- Voltage divider optimisation
- Improved from $<70\%$ to $\sim 80\%$



SuperNEMO Calorimeter R&D: PMTs

- **Photocathode uniformity:**

- Close collaboration with Hamamatsu to improve photocathode uniformity across the entire surface of the PMT



- **Timing:**

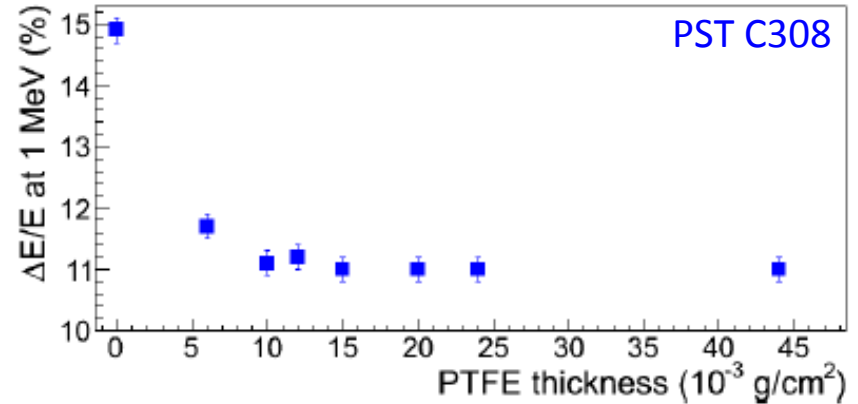
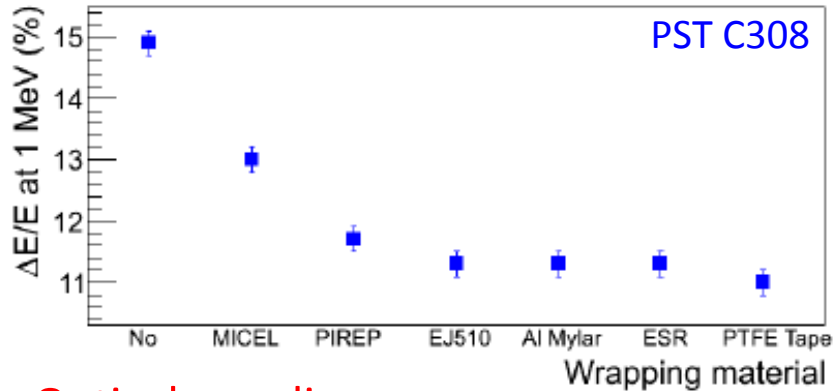
- Reducing the number of dynode stages improves the timing of the PMT by reducing the time transition spread (TTS)

- **Gain and Linearity** (a big achievement!):

- Reducing the number of dynode stages and optimising the voltage divider **decreases** the **gain**: $\sim 1 \times 10^5$
→ **Good linearity** (< 2% for very high light levels) whilst good gain of the 1st dynode and therefore high collection efficiency

SuperNEMO Calorimeter R&D: Reflective Material & Coupling

- Reflective material:
 - High reflectivity, radiopure, low Z and low density (to reduce backscattering)

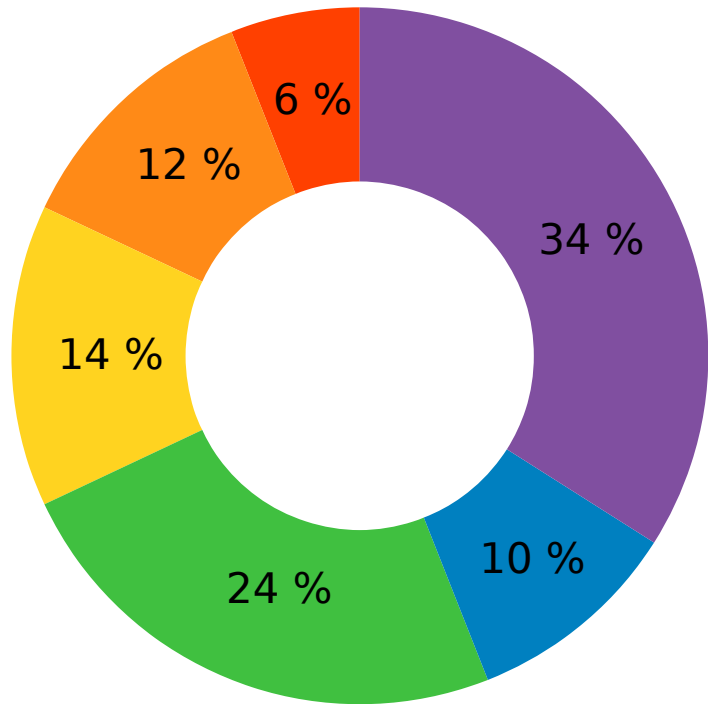


- Optical coupling:
 - Good optical coupling between scintillator and PMT essential for uniform and complete light collection

Optical Material	Refractive Index	$\frac{\Delta E}{E}$ (%)	f_{FWHM}
Alcohol	1.37	9.4 ± 0.2	1.
Gel	1.46	8.6 ± 0.2	1.08 ± 0.3
Gel	1.52	8.4 ± 0.2	1.11 ± 0.3
RTV 615	1.41	9.4 ± 0.2	1.00 ± 0.3

- Direct coupling of PMT to hemispherical cutout in scintillator gave the biggest impact in energy resolution improvement.

SuperNEMO Calorimeter R&D: Summary



Scintillator

- Geometry
- Surface (polishing + reflector)
- Material PS → PVT

Photomultiplier

- Quantum efficiency
- Optimisation of operation
- Changing 5" → 8" and direct coupling

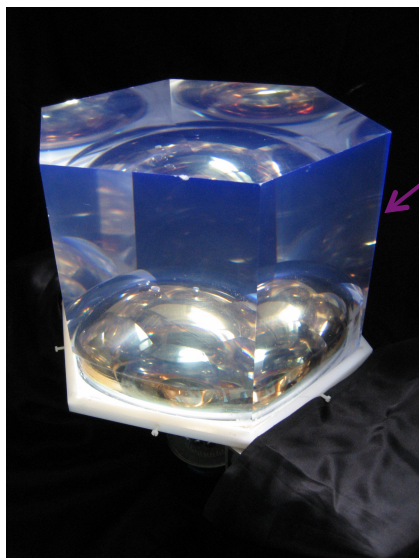
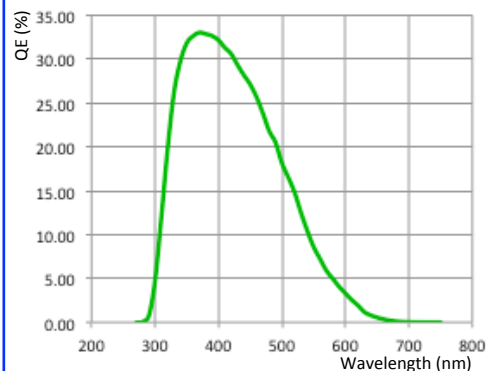
Optimised SuperNEMO Optical Module Design

EJ-200 hexagonal PVT block:

276 mm diameter
193 mm deep, minimum
thickness between PMT and
scintillator: 100 mm

R5912-MOD Hamamatsu 8" PMT:

Maximum quoted QE: 33%
32% QE at 400 nm



Wrapping:

Sides: 75 μm of PTFE (Teflon) ribbon
Sides and entrance face: 12 μm of Mylar

$$\frac{7.5\%}{\sqrt{E(\text{MeV})}}$$

Back to Proton Therapy...

- With this fantastic energy resolution of **7.5% FWHM at 1 MeV** can we apply the SuperNEMO optical module technology to proton therapy beam monitoring and proton imaging?

Challenges: from SuperNEMO (electrons) to a proton beam

- Very **high intensity** of events at a **proton beam** (~25 MHz):
 - A proton beam delivers a random number of protons per bucket, which will worsen the energy resolution measured
 - We require **1 proton per bucket** for a good detector response
- **Scintillator quenching** for **protons**:
 - For a plastic scintillator, the **scintillator response** is **nonlinear** with the amount of energy deposited in it
 - Amount of deviation → “quenching”
 - Characterised by Birk’s law:
$$\frac{dY}{dx} = \frac{S}{1 + kB(dE/dx)} \times \frac{dE}{dx}$$

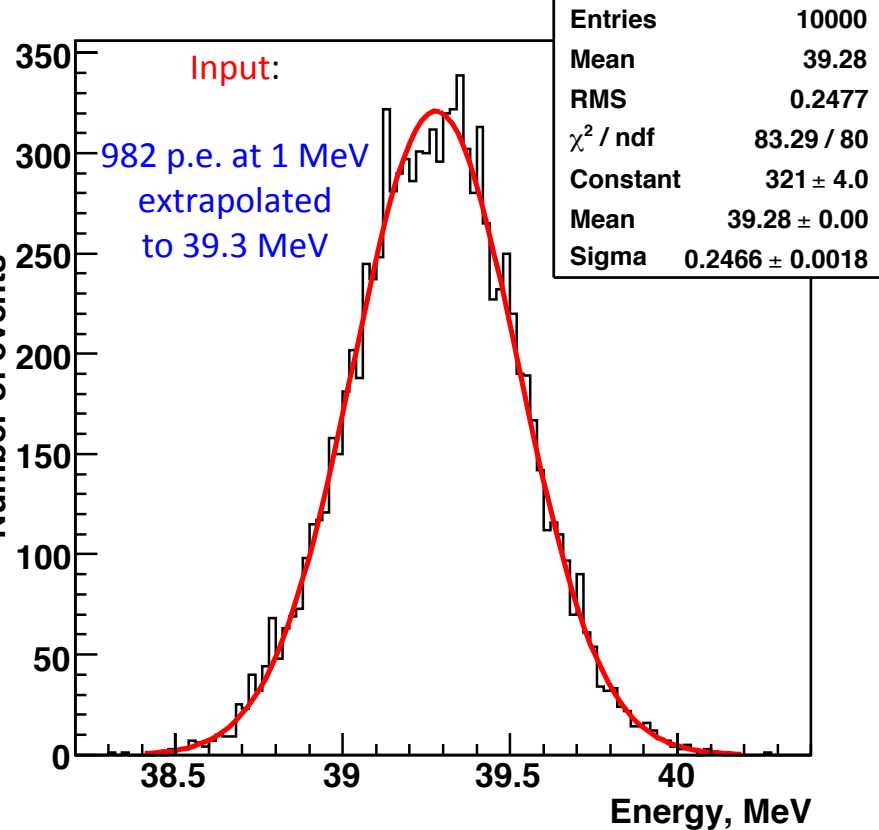
dY/dx	light yield per unit path length
dE/dx	energy lost by particle per unit path length
kB	relates density of ionisation to energy loss = 0.207 mm/MeV
S	absolute scintillation efficiency
 - Becomes important for **large dE/dx** and **ionisation density** → important for protons, which have a large dE/dx when they slow down
- **Energy range**:
 - **SuperNEMO** optimised for electrons from **0.5 – 4 MeV** for double beta decay
 - For **proton therapy** we require ~O(**100 MeV**)

Step 1: GEANT4 Simulations

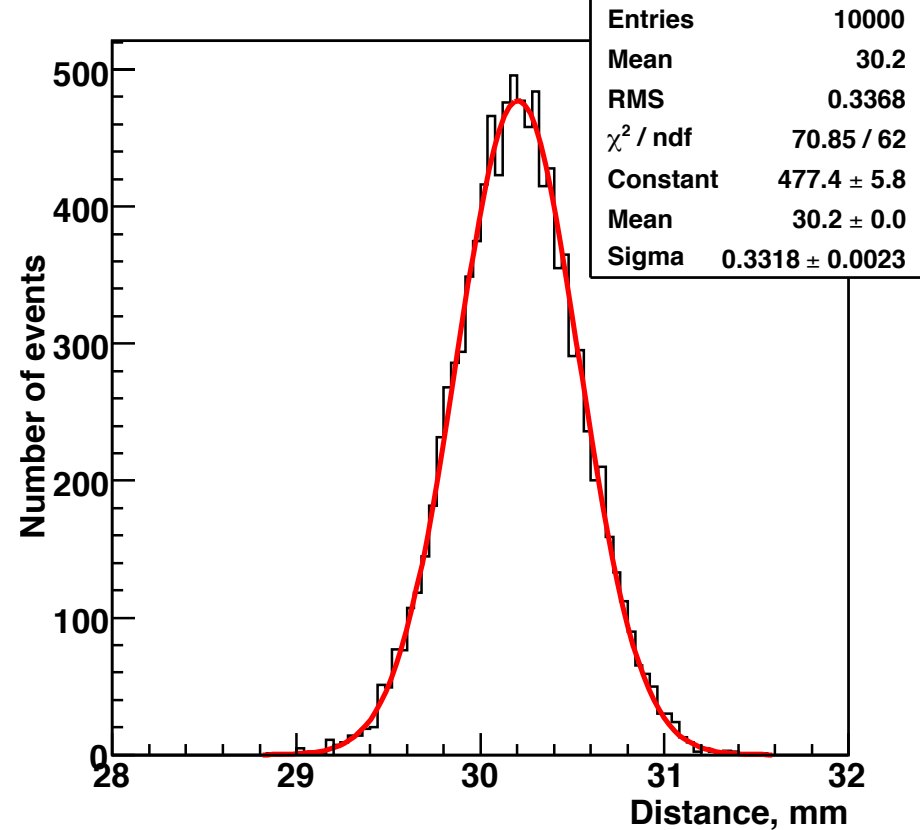
- A pencil **proton beam** (60 MeV) simulated, positioned 70 cm underneath the entrance face of the scintillator block
- Scintillator modeled as a **square** block (256 mm x 256 mm x 120 mm) with scintillator composition fully described
- **Quenching** of scintillation light in plastic scintillator for protons
- Energy deposited smeared according to **Poissonian fluctuations** in the number of generated photo-electrons
- The number of photo-electrons at per MeV taken from test bench data (SuperNEMO calorimeter R&D): **982 photo-electrons per MeV** (for an energy resolution of 7.5% FWHM at 1MeV)

Step 1: GEANT4 Simulations

Energy Deposited in Scintillator



60 MeV Proton Stopping Distance



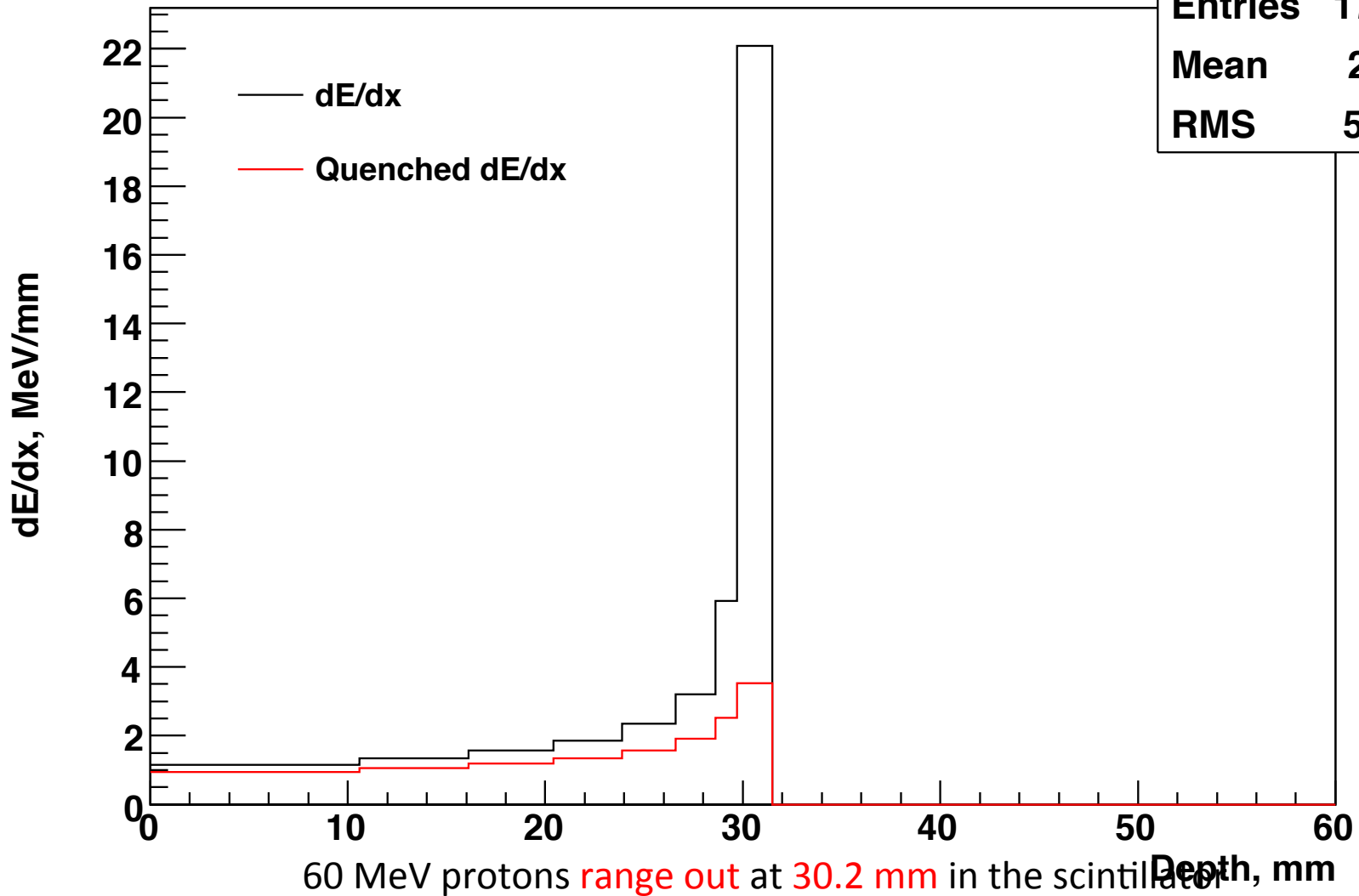
- **Quenching** from simulations:
 - Simulated mean: 39.3 MeV
 - Quenching: **35% for 60 MeV protons**

- **Energy resolution** from simulations:
 - $\sigma: 0.247, \mu: 39.28$
 - $\Delta E/E: 1.48 \% \text{ FWHM}$

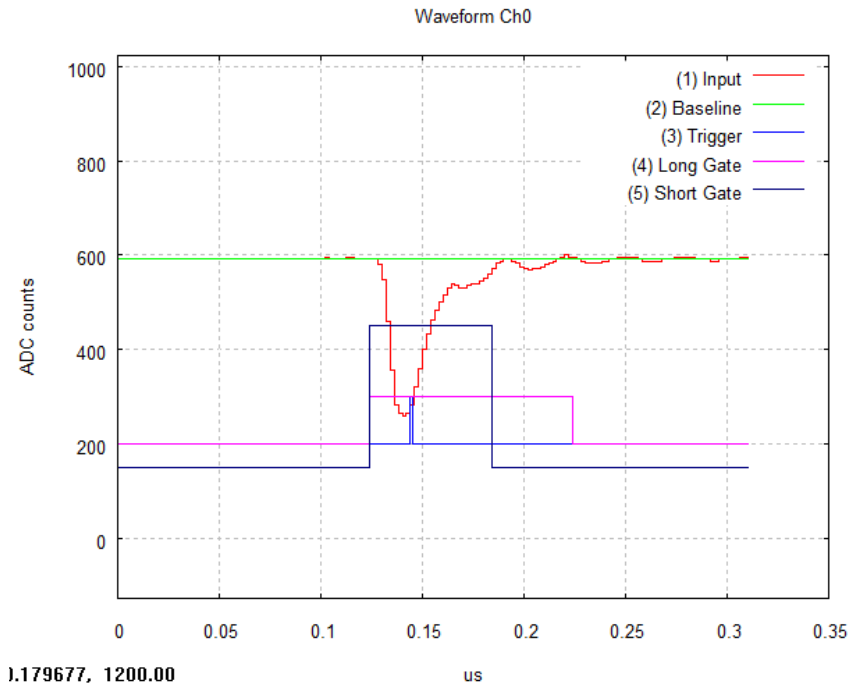
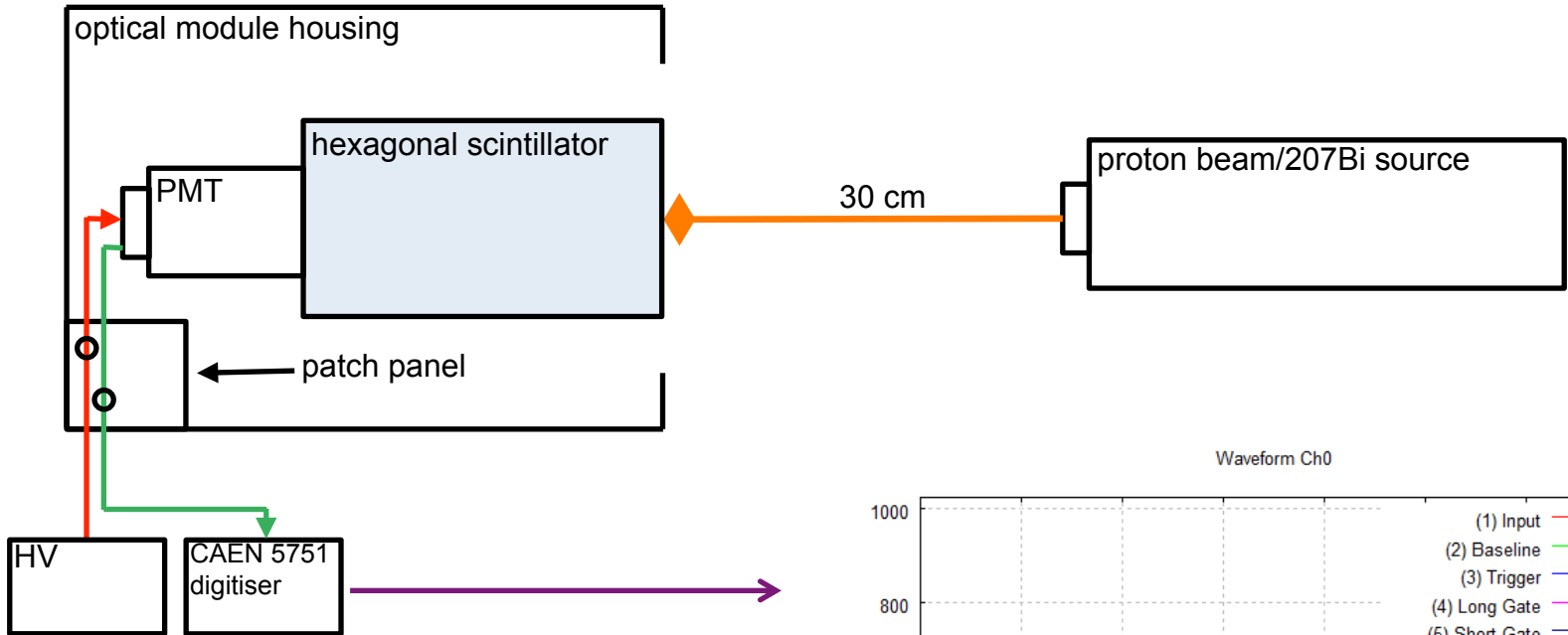
$$\frac{\Delta E}{E} = \frac{2.35\sigma}{E}$$

Step 1: GEANT4 Simulations

dE/dx as a Function of Depth



Step 2: Equipment Setup



CAEN DT5751 Digitiser:

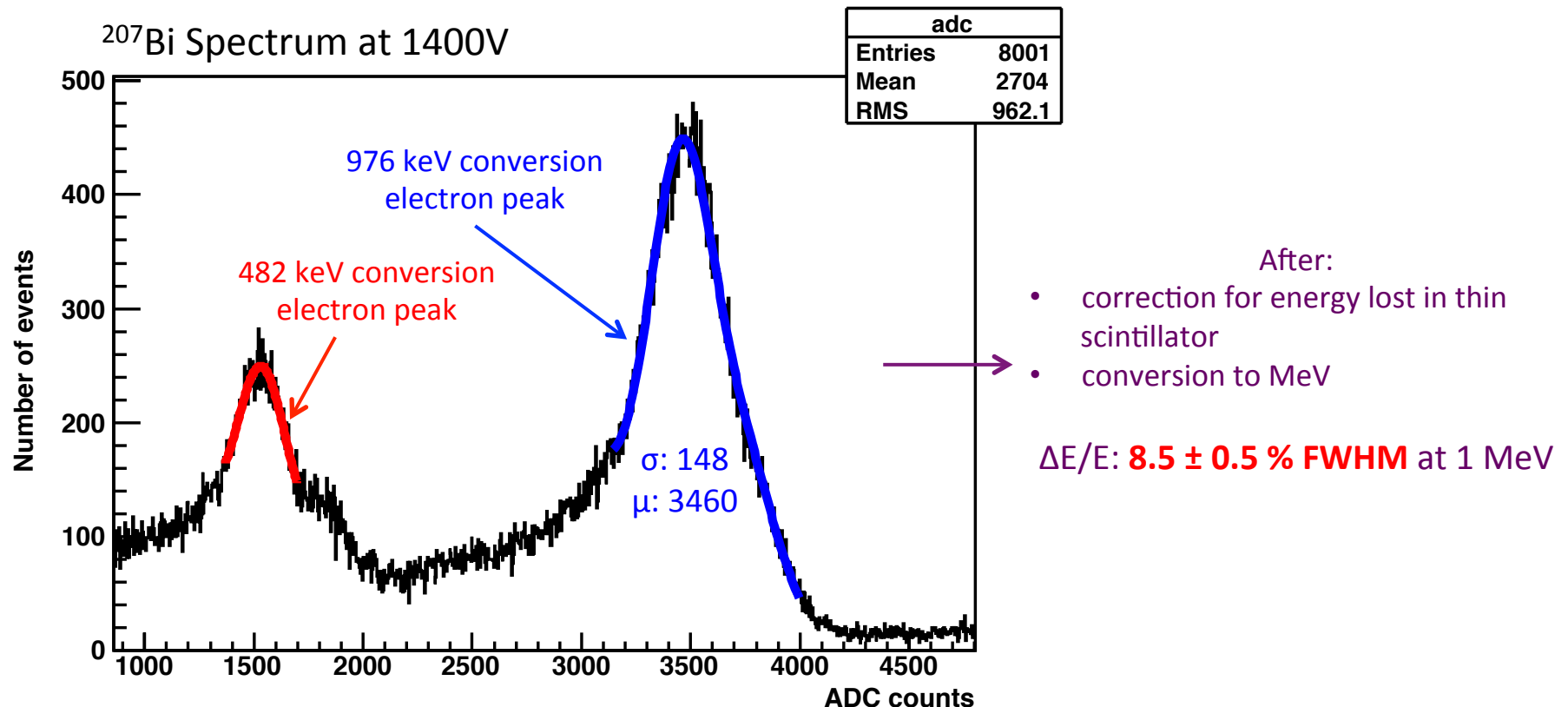
Dual-gate signal integration

→ On-the-fly pulse shape analysis

→ Neutron/gamma discrimination

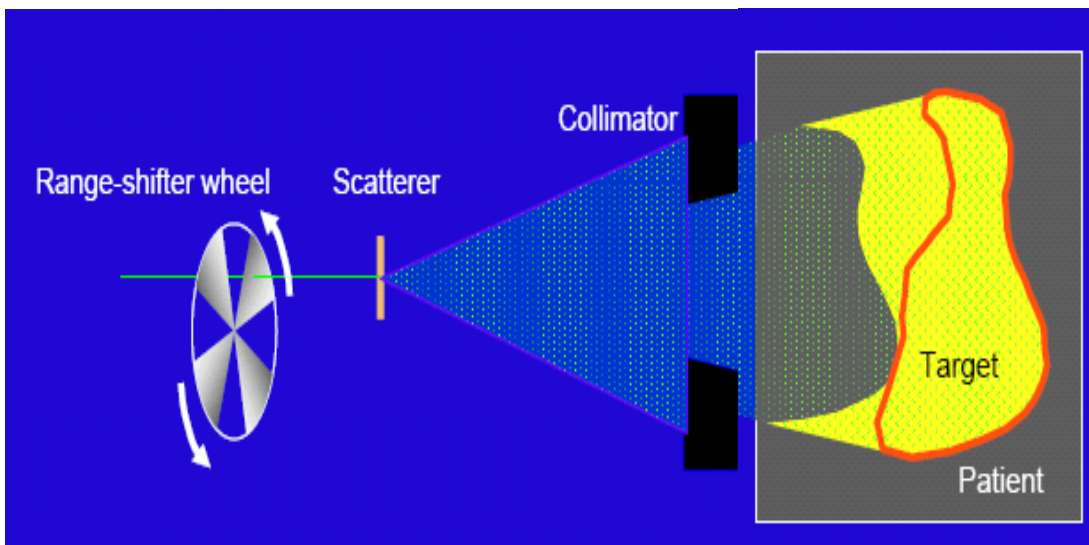
Step 3: ^{207}Bi Test at UCL

- Optical module resurrected after some years: re-measure energy resolution!
 - New test bench at UCL: a thin scintillator introduced into set up, which triggers DAQ only when an electron passes through it
 - Gammas removed, fit simplified to **triple Gaussian** of 976 keV and 482 keV peaks



Step 4: Clatterbridge Cancer Centre

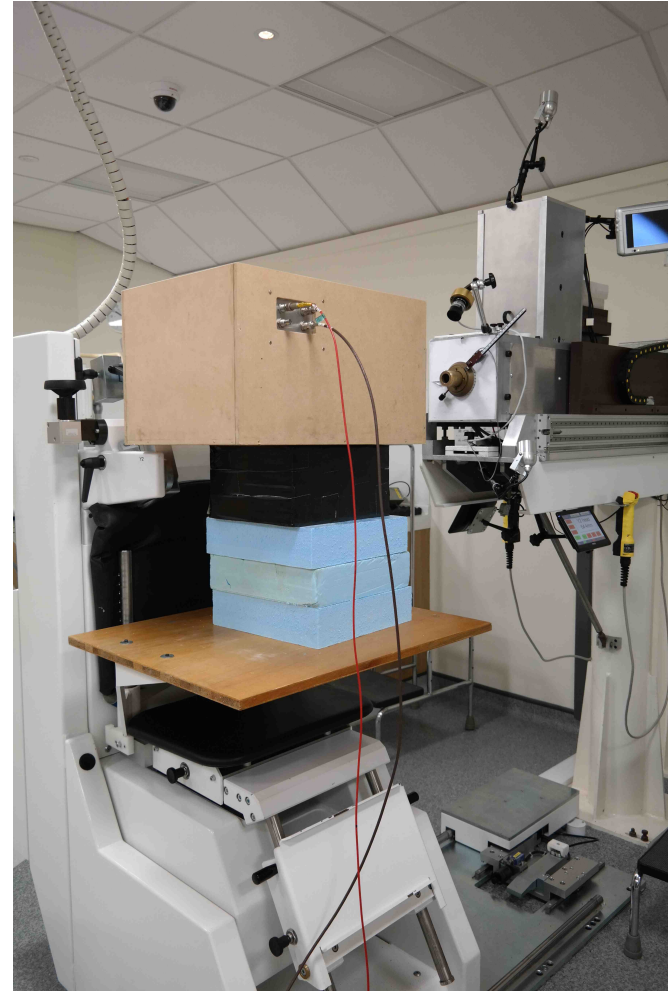
- Only currently operational proton beam treatment centre in the UK
- Home to the **Douglas Cyclotron** → produces **60 MeV proton beam** for the treatment of ocular melanomas (penetration of 60 MeV protons: 31 mm in water)
- **Double scattering** beam technique:



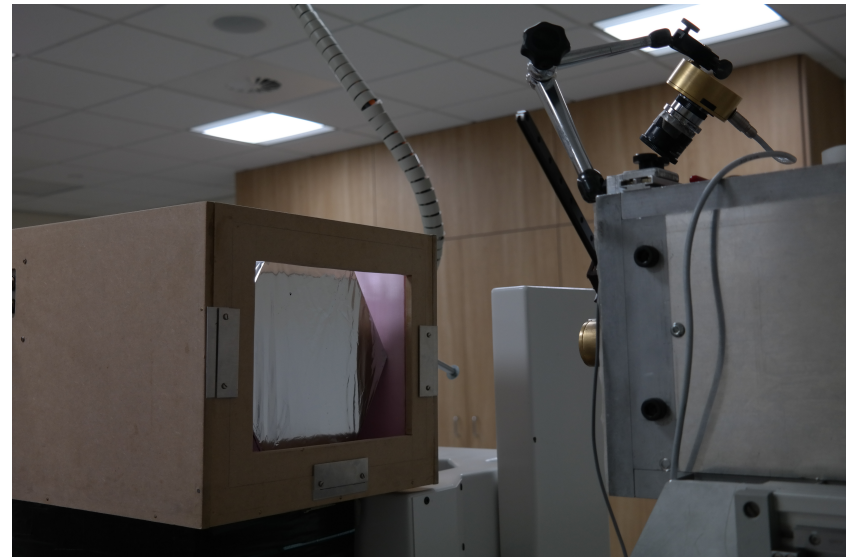
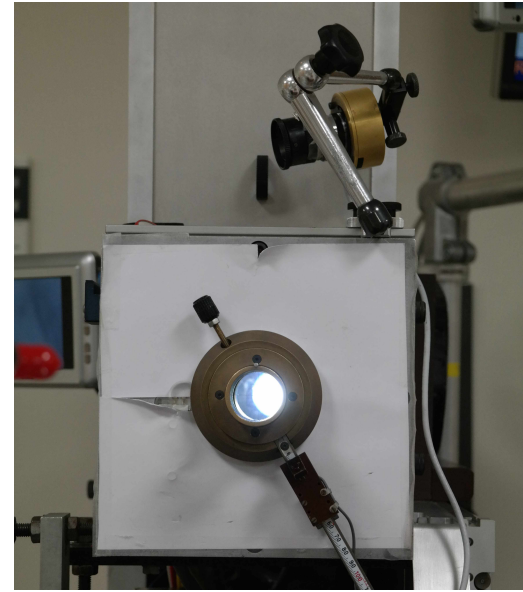
- Beam accelerated to **single energy**
- Beam passes through **range-shifter wheel** that modulates the proton beam energy to reach front/back of target volume
- **Scatterer** enlarges beam to cover whole volume
- **Collimator** shapes outer edge of beam to target area

Step 4: Clatterbridge Cancer Centre

- **Four** full days in total of proton beam access granted to UCL in December 2013 and December 2014



Step 4: Clatterbridge Cancer Centre

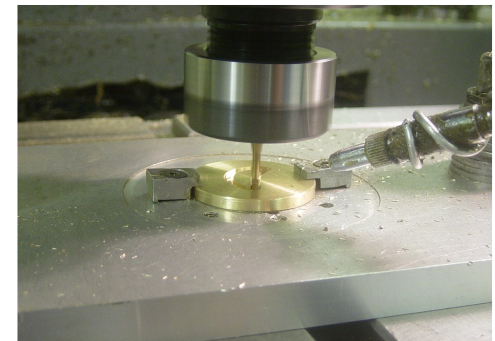


Step 4: Clatterbridge Cancer Centre



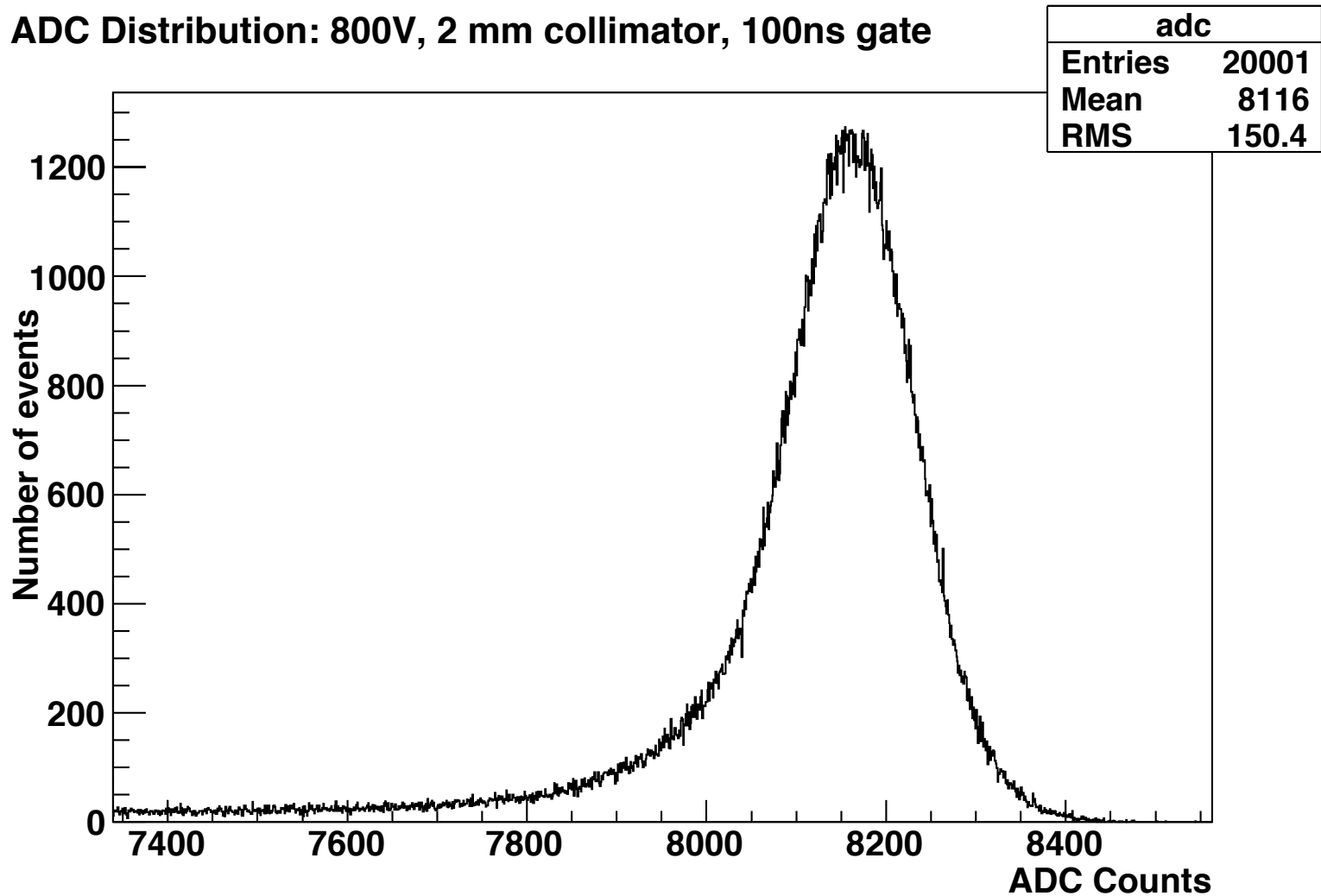
Step 4: Clatterbridge Cancer Centre

- The proton rate from the beam was carefully controlled by:
 - Inserting brass **collimators** with **varying diameters** (0.5 mm – 10 mm) into the beam nozzle (~30 cm upstream of the optical module)
 - Adjustment of the **ion source gas supply**
 - Adjustment of the **discharge current**
 - Adjustment of the **cyclotron RF phase**
- Over the four days of test beam the dependence of measurements on the following parameters was studied:
 - Collimator diameter size (0.5 mm – 10 mm)
 - Beam settings
 - Operating voltage of the PMT (800 V, 900 V)
 - **Increasing HV increases collection efficiency** of the PMT and therefore achieves a better energy resolution
 - Note: standard operating HV for this PMT is 1500V, but due to such high light levels (100,000 photons → **30,000 photo-electrons**)
 - Integrating window of acquisition on the CAEN digitiser (50 ns, 100 ns, 200 ns): sensitive to pile up effects



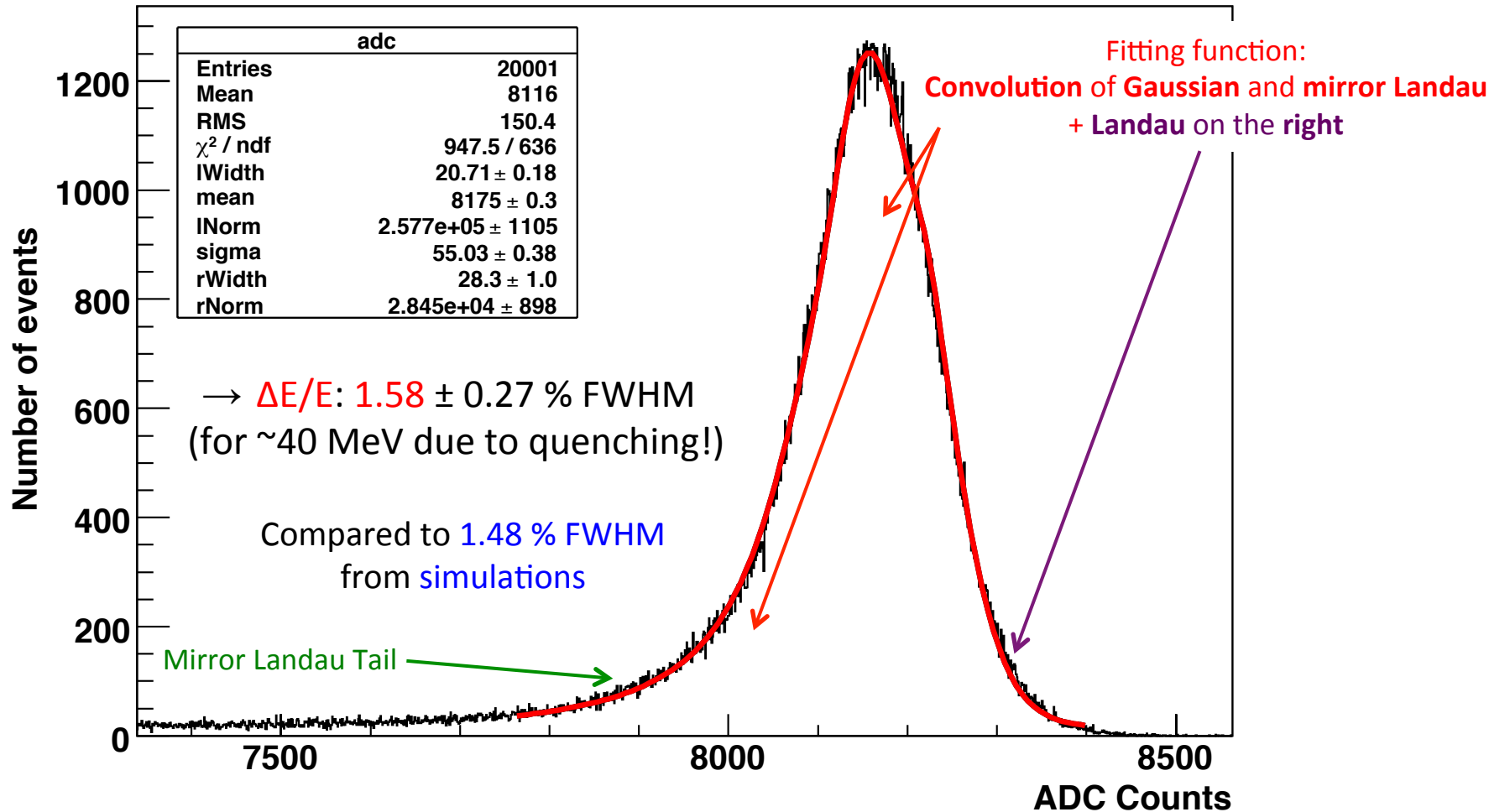
Step 4: Clatterbridge Cancer Centre

ADC Distribution: 800V, 2 mm collimator, 100ns gate



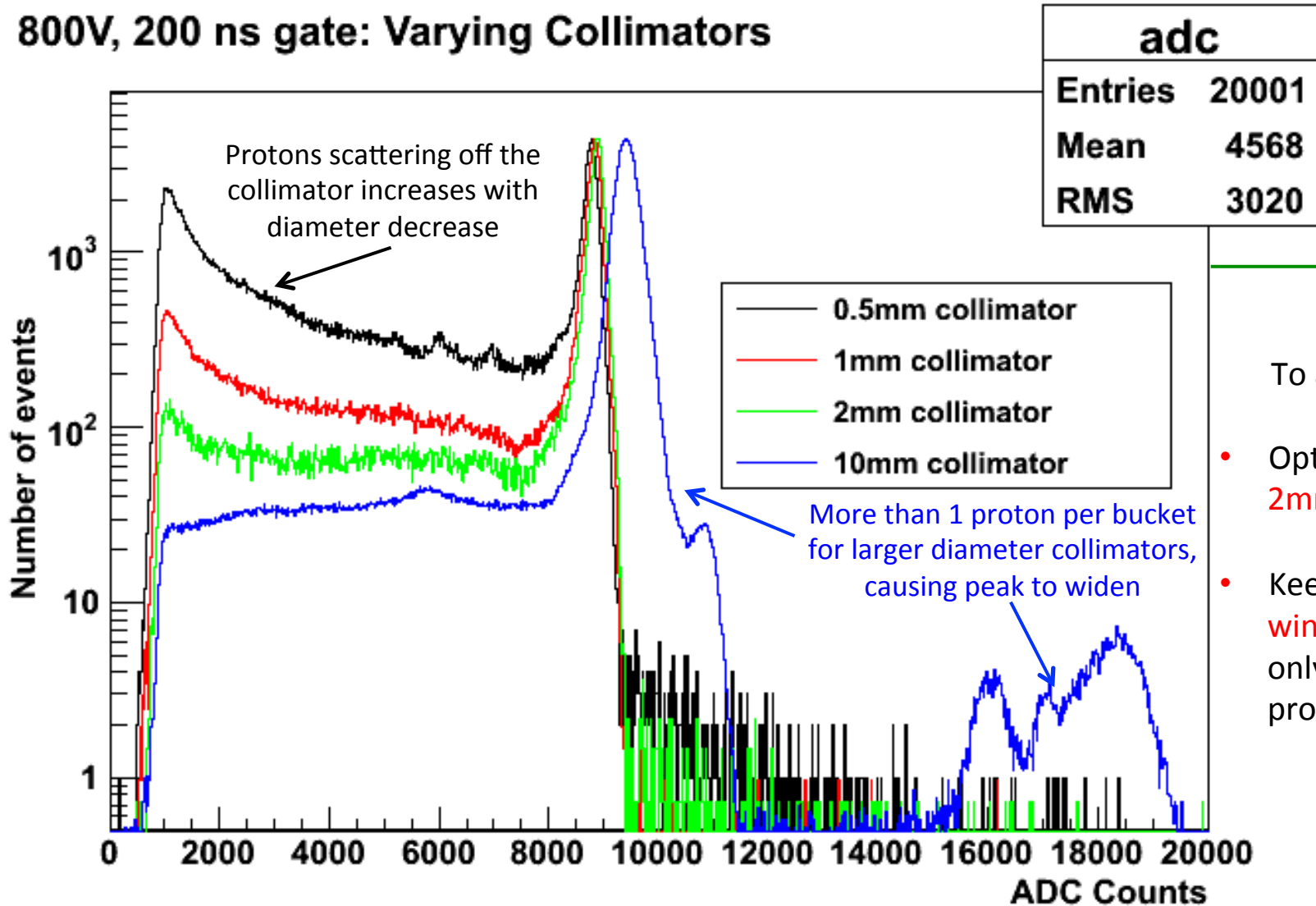
Step 4: Clatterbridge Cancer Centre

ADC Distribution: 800V, 2 mm collimator, 100ns gate



Pile Up: Varying Collimators

800V, 200 ns gate: Varying Collimators



Considering Measuring Parameters

PMT HV (V)	Acquisition window (ns)	Collimator diameter (mm)	Energy resolution, % FWHM
800	50	2	1.6 ± 0.18
800	100	2	1.58 ± 0.27
800	200	2	2.11 ± 0.42
900	50	2	1.1 ± 0.13
900	100	2	0.97 ± 0.16
900	200	2	1.27 ± 0.19
800	200	3	2.32 ± 0.43
800	200	4	2.16 ± 0.41

Reducing the acquisition gate from 200ns to 100ns shows considerable improvement (ensures we only look at 1 proton).

But we don't win anything with a 50ns gate.

At 900 V:

Improved energy resolution but are we linear at 900 V? (See later)

Further confirmation that 2mm diameter collimator is optimal for reducing intensity

Our optimal parameters for measurements are:

PMT HV: 800 V

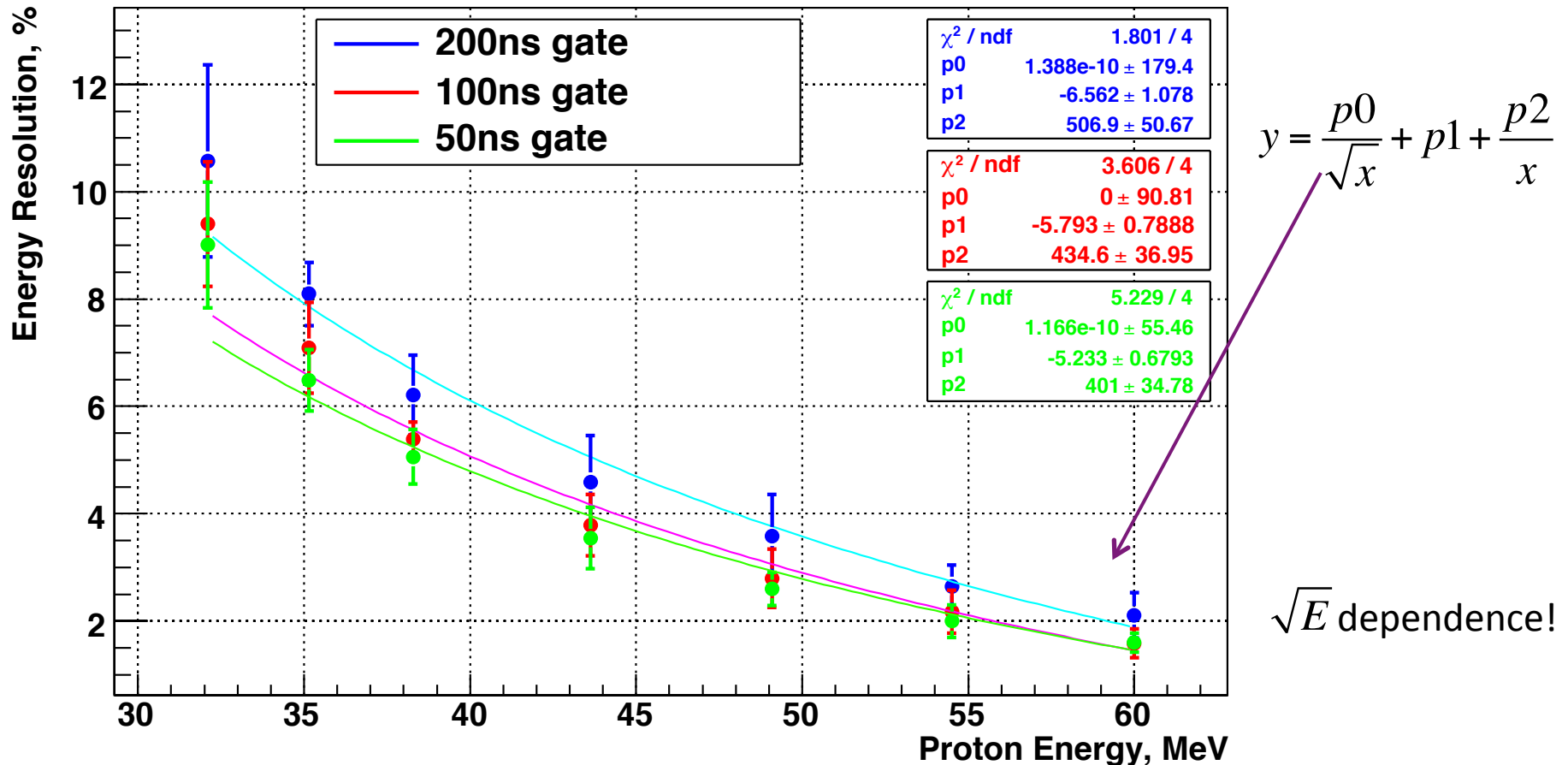
Acquisition window: 100 ns

Collimator diameter: 2 mm

Energy Dependence on Resolution

- Energy of protons incident on scintillator varied by placing absorbers (PMMA plates) of known thickness ~ 1.8 m upstream of the optical module

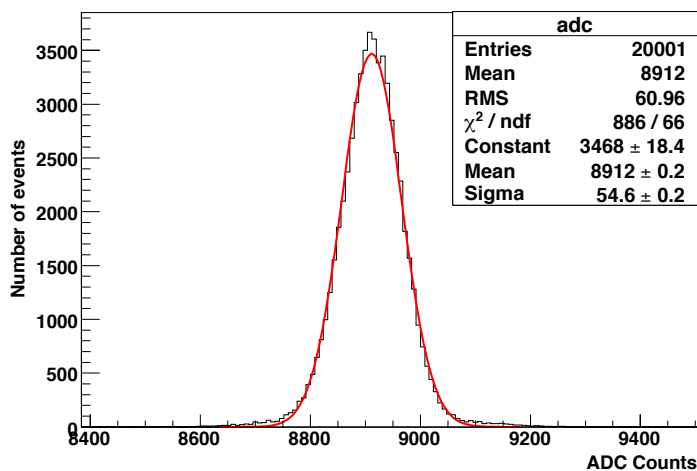
Energy Resolution as a Function of Proton Energy: 800V



Intrinsic Energy Resolution of Optical Module

- How much of the measured energy resolution is due to the proton beam and how much is due to the “intrinsic” energy resolution of the detector?
- From MC (1.48%) we already know that most of the energy resolution measured with the proton beam (1.58 ± 0.27) is from the intrinsic resolution of detector:
 - Use MC and data to put a limit on the energy spread of the 60 MeV Clatterbridge beam:
Proton energy spread: 0.65 ± 0.66 % FWHM
or limit on spread: **FWHM (60 MeV): $<1.56\%$ at 90% CL**
- Also tests carried out at UCL:
 - Pulse PMT with a 400nm LED at an amplitude and width that will give a peak at the same ADC counts as the proton beam spectra
 - Fit the acquired spectra with a Gaussian and extract energy resolution

LED Pulsed Distribution for 800V, 200 ns and 60 MeV Proton Beam

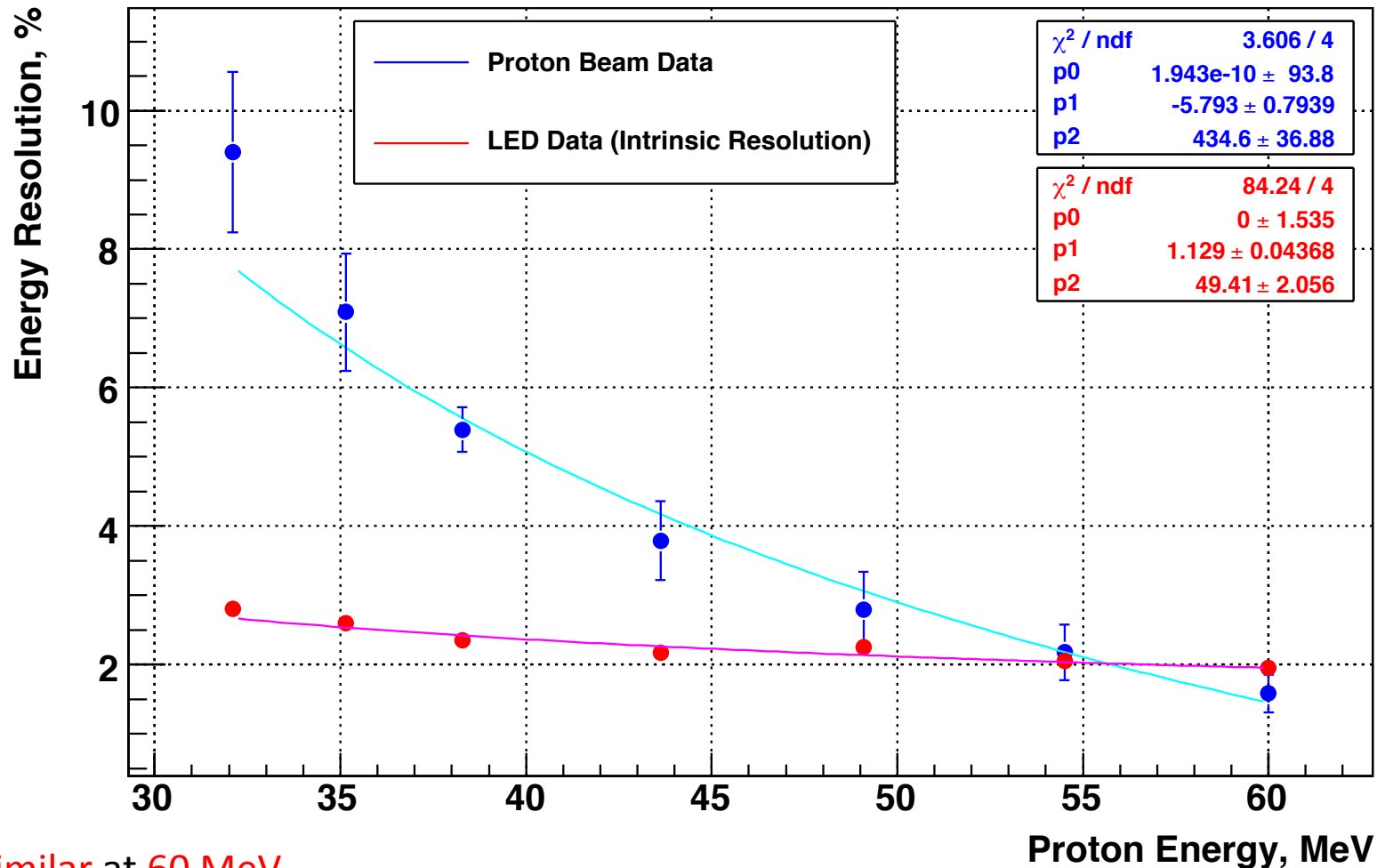


→ BUT: LED is operating at very “high” parameters (~8V and 40ns width), therefore the width is very sensitive to noise and the LED distribution would be better monitored with a device such as a pin diode

→ future measurement!

Intrinsic Energy Resolution of Optical Module

Energy Resolution as a Function of Proton Energy: 800V, 100ns gate

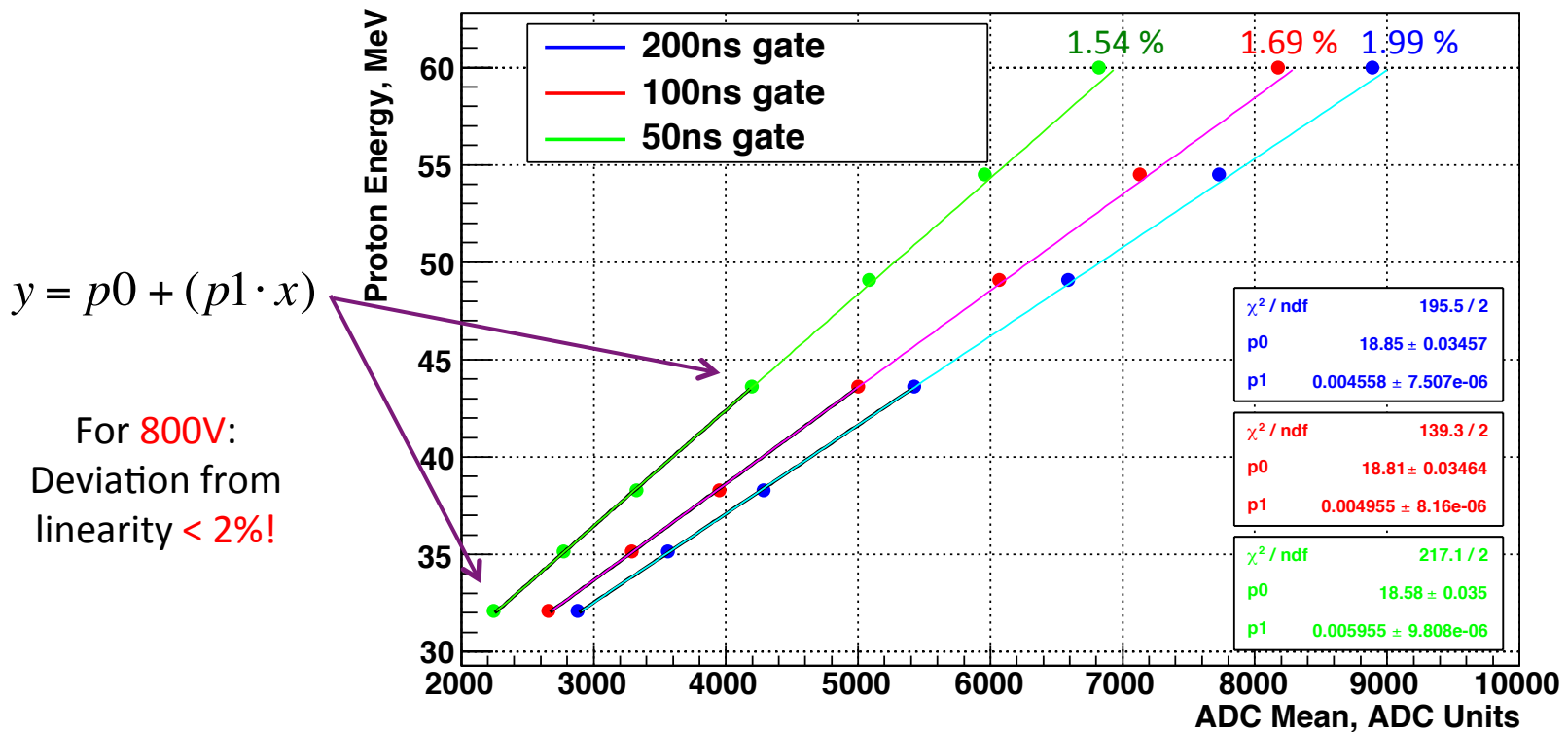


- Similar at 60 MeV
- Proton beam energy resolution much worse than intrinsic energy resolution at lower energies due to scattering of protons

Linearity: 800 V

- We want to run the PMT at **higher voltages** (can run at up to 1500V) as this will **increase** the PMT's **collection efficiency** and will improve the energy resolution: $0.97 \pm 0.16 \% \text{ FWHM}$ from measurements (900V, 100 ns gate)
- BUT we have a **LOT of light** (tens of thousands of photo-electrons): can we trust this result?
 - Look at **linearity**

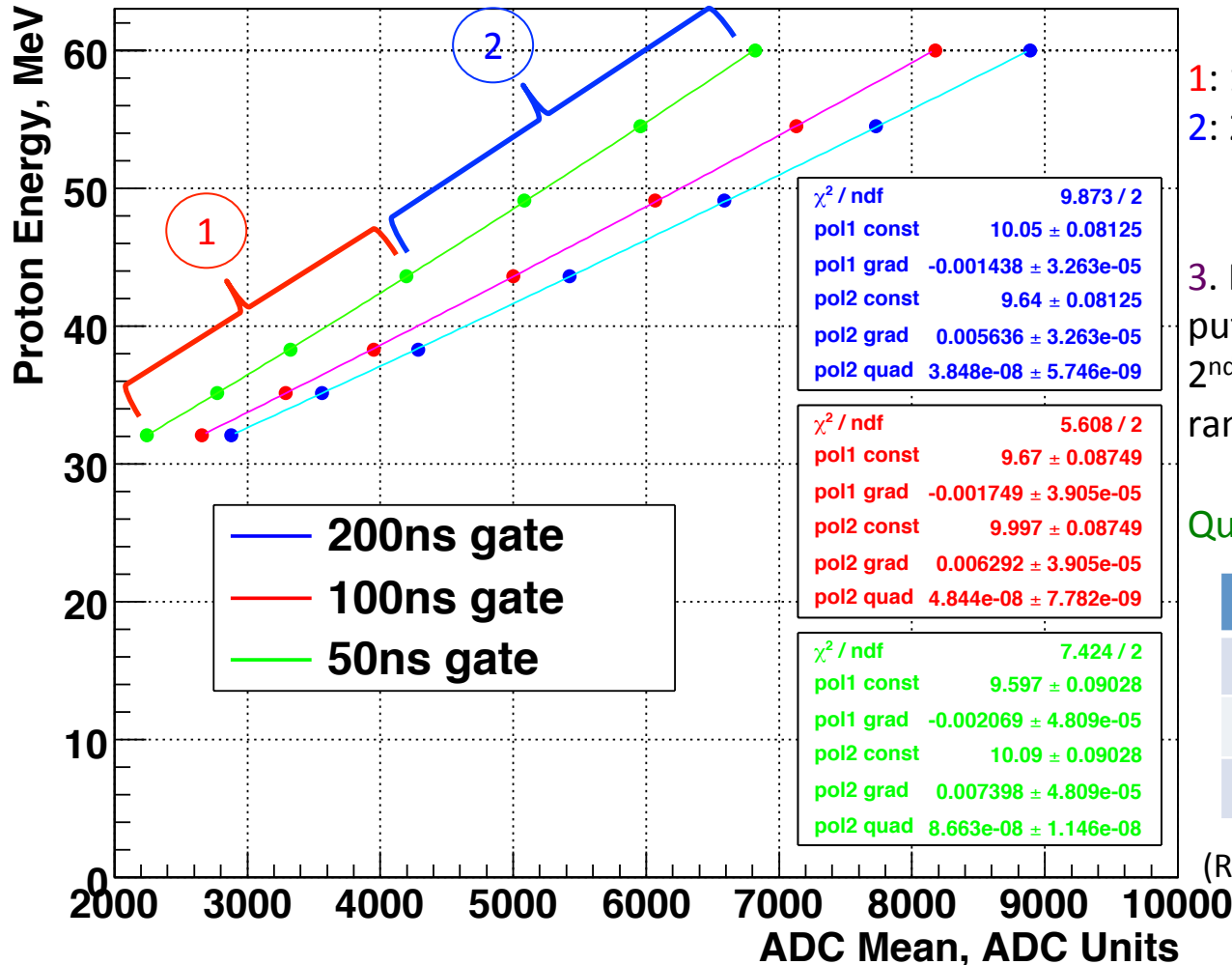
Proton Energy as a Function of ADC Mean: 800V



Measuring Quenching

- Fitting linearity curves gives us a measurement of scintillator quenching:

Proton Energy as a Function of ADC Mean: 800V



Fitting procedure:

- 1st degree polynomial (32-44 MeV)
- 2nd degree polynomial (44-60 MeV)

3. Parameters extracted from 1 and 2 put into "combined" 1st degree and 2nd degree polynomial over entire range

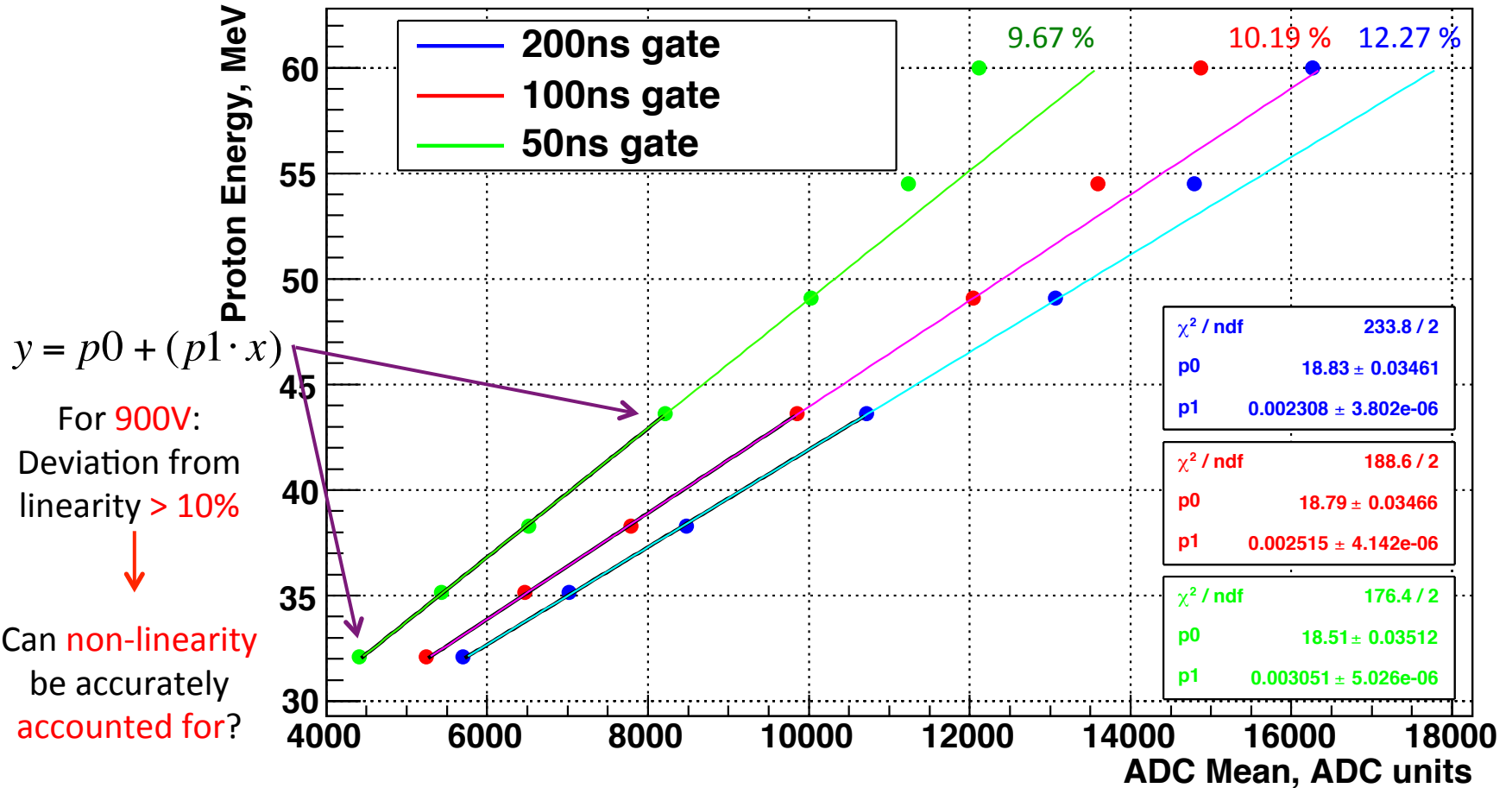
Quenching = pol1 const + pol2 const

Gate (ns)	Quenching (MeV)
50	19.69 ± 0.12
100	19.67 ± 0.12
200	19.69 ± 0.13

(Remember: 20.57 MeV from simulations)

Linearity: 900 V

Proton Energy as a Function of ADC Mean: 900V



“Unfolding”: Getting a Grip on Non-Linearity

- For our 900 V data we see non-linearity > 10 %
- BUT can we take into account non-linearity of our equipment to “unfold” the true energy resolution?
- We want to be able to do this:
 - To potentially increase HV even further (to 1000 V or above) to increase collection efficiency and hence improve the energy resolution
 - For proton imaging: requires protons > 300 MeV, which will give a huge amount of light and non-linearity will be inevitable
- Work currently on-going to determine the best way to:
 - Convert the data from ADC counts to MeV (“visible energy” due to quenching)
 - Fit the visible energy data to extract the “unfolded” energy resolution (with non-linearity taken out)
 - Compare results for 800 V and 900 V

Future Plans

1. We already have a great result for energy resolution, but can we push it any further?

- Use the same technology, but **reduce in size** to allow us to **collect more light**
- Use 3" UBA (43% QE) Hamamatsu PMTs used for SuperNEMO calorimeter R&D coupled to small EJ-200 scintillator. Two scintillators ordered:

Block: 4 cm x 4cm x 5 cm

Cylindrical: 4 cm diameter x 5 cm

Entrance face area chosen to fully fit the 3" diameter PMT



- Test at UCL with ^{207}Bi and in the 60 MeV proton Clatterbridge beam

2. Given the amount of light we have (~30,000 photo-electrons), consider using **alternative photo-detectors**:

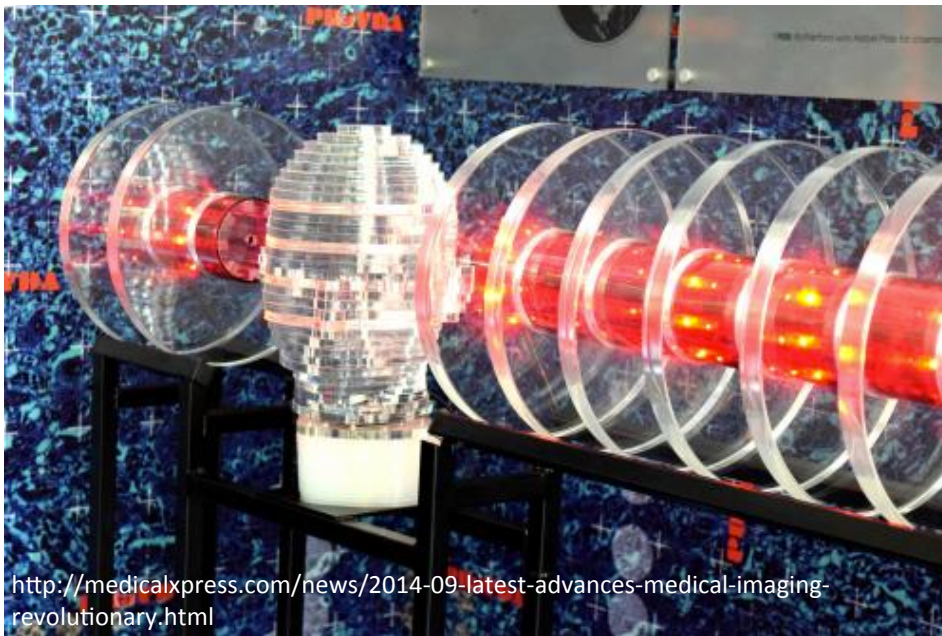
- High QE, low gain
- Removes any non-linearity
- CCD, SiPM, etc.

Future Plans

3. We need to think about **practical arrangements** for beam monitoring and proton imaging:

- Talk to **clinical scientists** and **medical physicists** at UCLH for specific design constraints needed to produce a deliverable product
- Collaborate with the **PRaVDA** (Proton Radiotherapy Verification and Dosimetry Applications) Consortium funded by the Wellcome Trust:

“The world’s first silicon-based detector system that will allow in-situ monitoring of the incident dose, in terms of its fluence, energy and distribution both prior to and during treatment.”



Silicon radiation hard detectors used for accurate tracking → from PRaVDA

Calorimetry with optical modules → from UCL

<http://medicalxpress.com/news/2014-09-latest-advances-medical-imaging-revolutionary.html>

Future Plans

4. Neutron background simulations and measurements:

- Protons create secondary fast neutrons from interaction with the beam pipe etc.
- This neutron background flux and spectra at proton therapy facilities is **poorly known**
- Must be measured to **avoid adverse biological effects** to the patient
- Try to use the same SuperNEMO technology to measure neutron flux and spectra

1. Collaborate with **dark matter colleagues** at UCL for neutron simulations

2. **Calibrate** the detector with a spectrum of known neutrons at the National Physical Laboratory (**NPL**) to get **detector response**

- Radionuclide sources for broad energy spectra or 3.5 MV Van de Graaf accelerator for monoenergetic neutrons
- Use pulse shape analysis provided by the CAEN DT5751 digitiser
- Make any modifications if necessary
- Apply detector response in simulations

3. Measure the neutron rate and spectrum at **Clatterbridge**



<http://www.npl.co.uk/measurement-services/neutron-measurements/>

Summary & Conclusions

- An optical module designed for the SuperNEMO experiment has measured the 60 MeV proton beam at Clatterbridge with an energy resolution of:

1.58 ± 0.27 % FWHM
(for 40 MeV “visible” energy)



simple extrapolation:

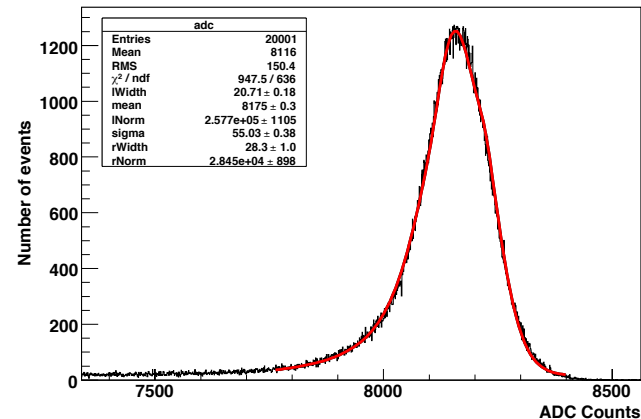
0.7 % FWHM @ proton imaging energy (300 MeV)

Limit on energy spread of Clatterbridge beam:

$\text{FWHM (60 MeV)} < 1.66\%$ @ 90% CL

- An important result for the future of proton beam monitoring and proton imaging
- Lots to do!!!
 - Ongoing data analysis from four days of Clatterbridge test beam data in December 2013 and December 2014
 - Can we do better with the same technology reduced in size?
 - Alternative photo-detector technologies
 - Lots of collaboration with colleagues coming up!

ADC Distribution: 800V, 2 mm collimator, 100ns gate



Acknowledgements

- UCL participation in this work:

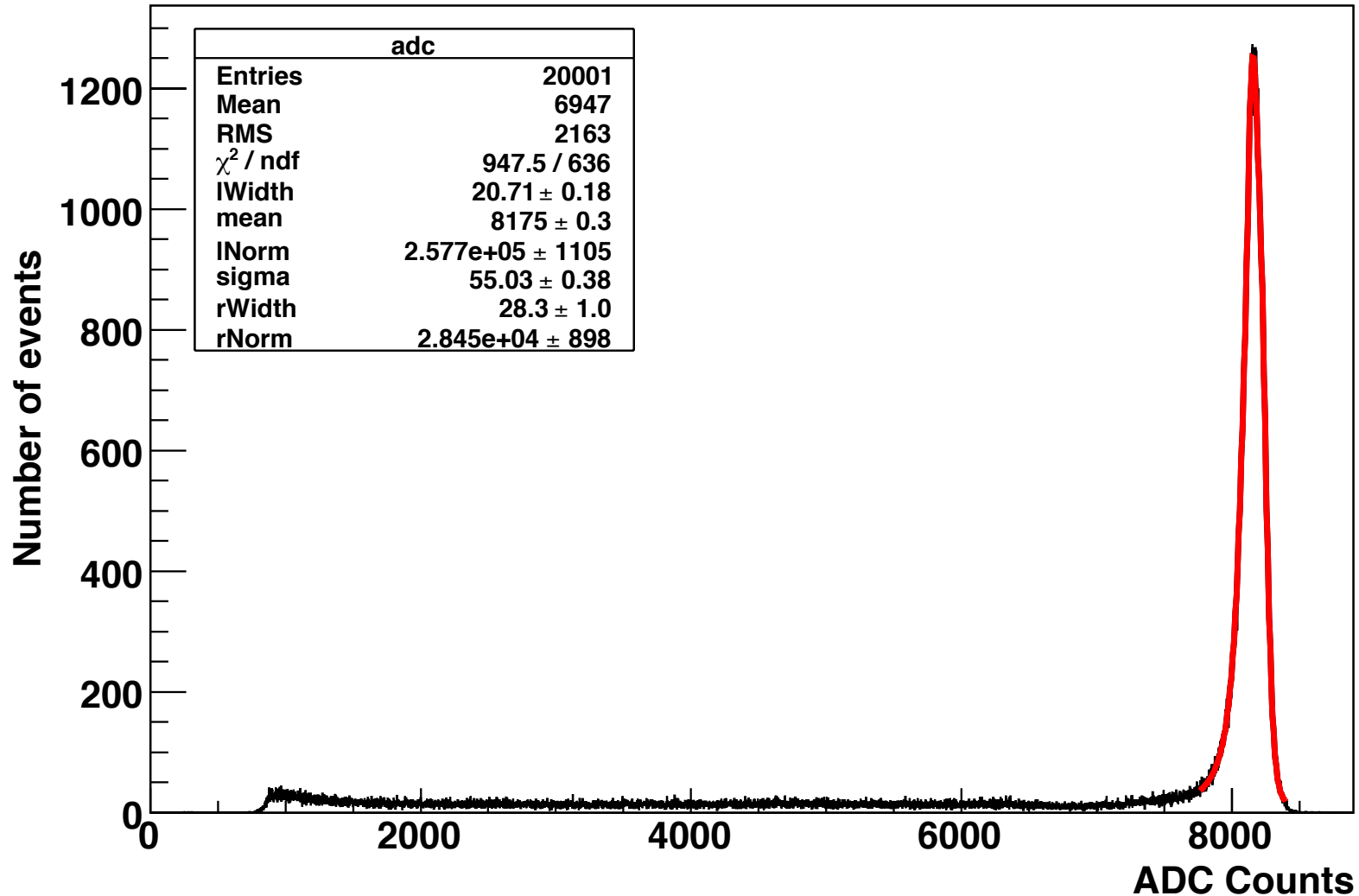
Simon Jolly, Ruben Saakyan, Derek Attree,
Anastasia Basharina-Freshville and Sophie Neal

- A HUGE thank you to **Andrzej Kacperek** and the fantastic **team at Clatterbridge** for all of their expertise and help!



Backup Slides

ADC Distribution: 800V, 2 mm collimator, 100ns gate



Backup Slides

ADC Distribution: 800V, 2 mm collimator, 100ns gate

