Radiotherapy : Beam monitoring in high-intensity radiotherapy treatments beams

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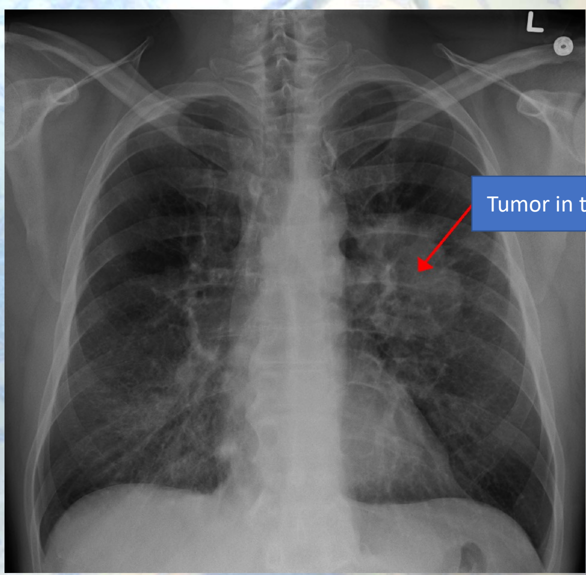
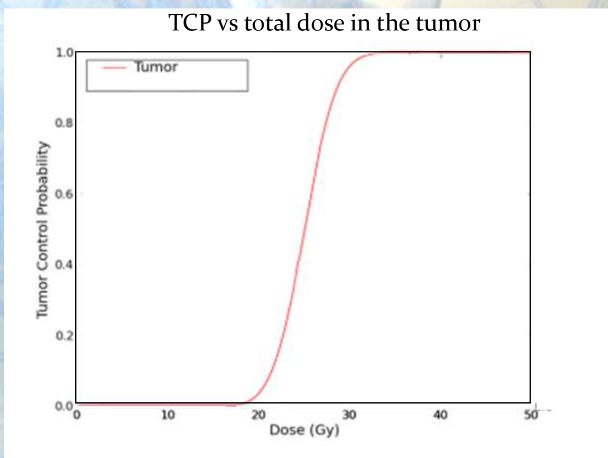
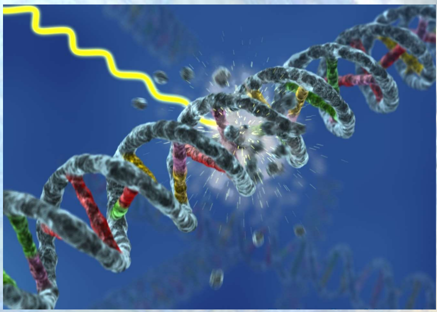
Cancer, what does it look like ?



Let's burn the tumor !

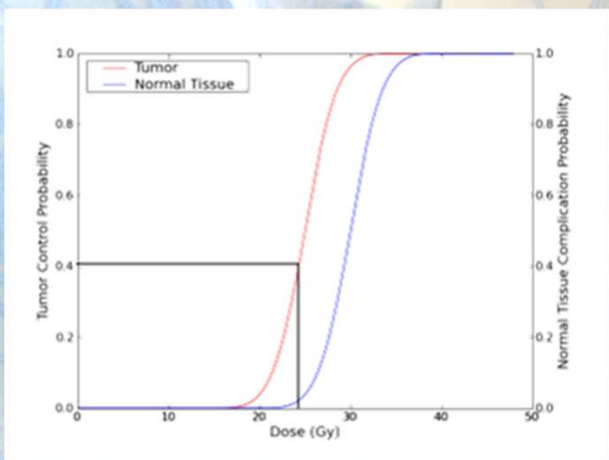


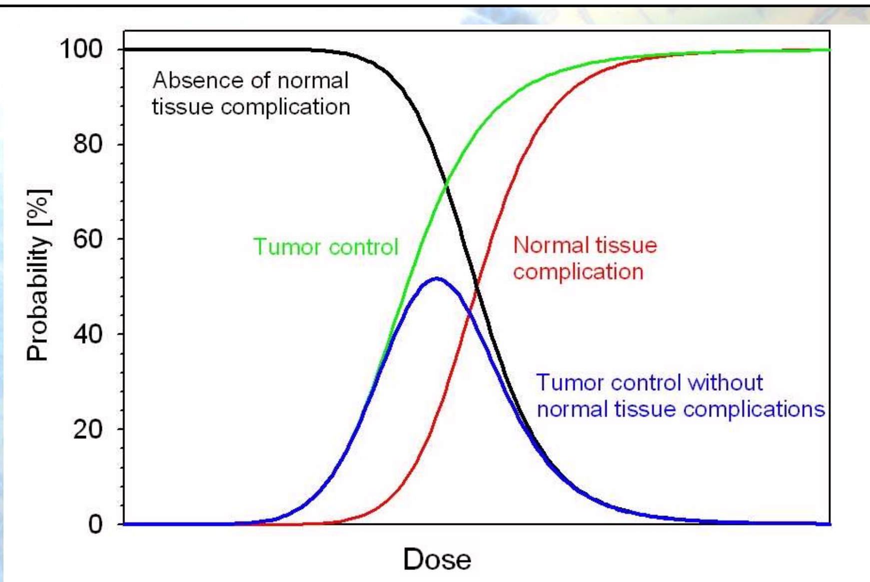
Create direct and indirect damages in DNA



External beam will deliver energy via particles to alter the DNA of target cells

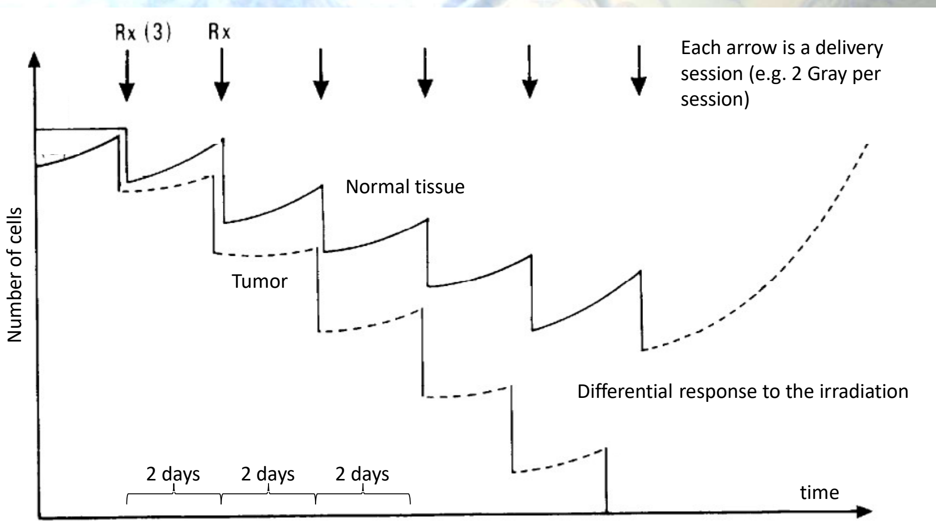
Slow down … as radiation also affects normal tissue





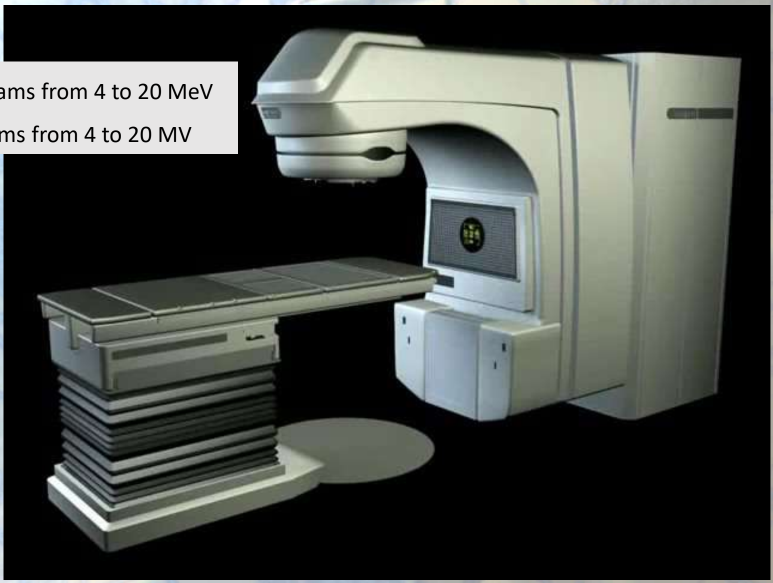
Overdosage > 5% might trigger normal tissue complications
Cancer cells might recover from an **underdosage > 5%**
Dose delivery windows is rather narrow

Dose fractionation



A compact Linear Accelerator to deliver the dose : **Linac**

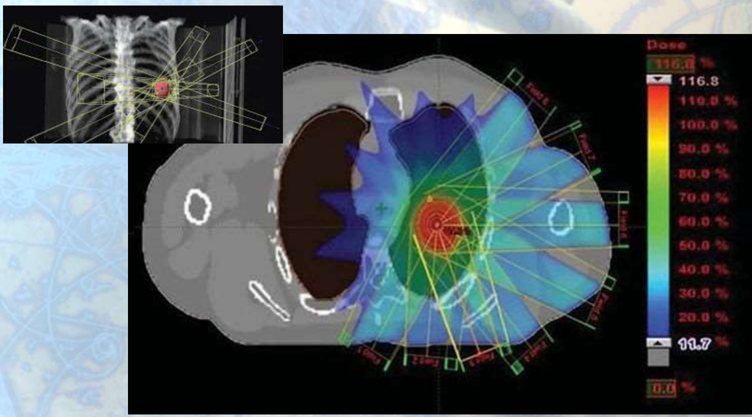
- electron beams from 4 to 20 MeV
- photon beams from 4 to 20 MV



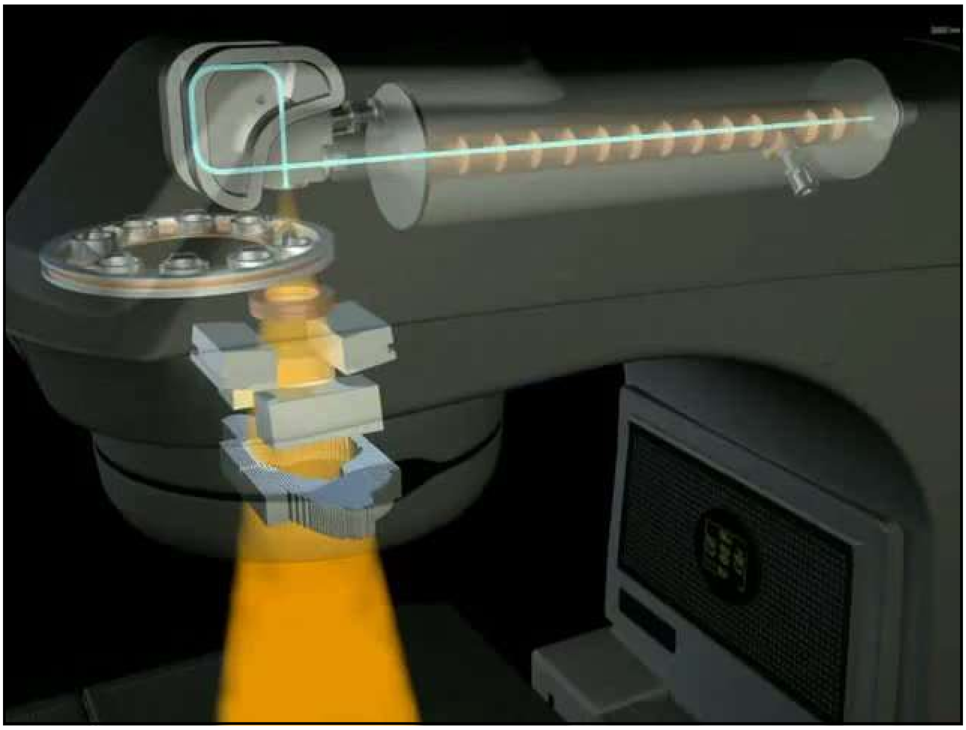
Deliver the prescribed dose in the tumor, with an extreme accuracy, all along the delivery sessions

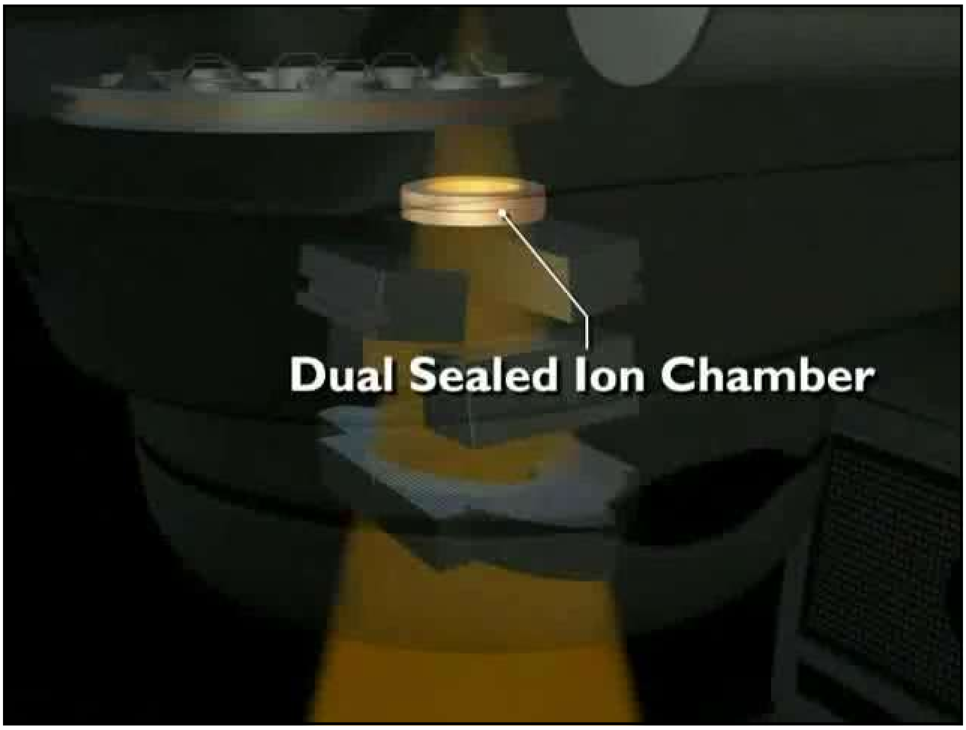
Anatomic model of patient from CT scan : tumor and other organs are localized.

Computer simulation to match the **dose prescription** from the radiotherapist



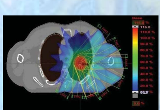
Multiple entry points : correct total dose in the target + protect the organs at risk





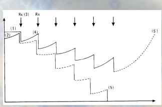
What about the dose ?

Got the Linac to deliver the photon beam ☑



Linac head will rotate
Multiple entry points to deliver the correct dose

Set a dose delivery of 2 Gray per session
(as set by the radiotherapist)



Btw : what is one Gray ?

What about the dose ?

What is one Gray ?

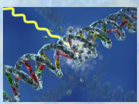
→ Def : absorption of one joule of radiation energy per kilogram of matter

Radiation produces ionization ($3/5^{th}$), excitation ($1/5^{th}$)

and other small energy transfers($1/5^{th}$).

All 3 components contribute to the absorbed energy

$$\boldsymbol{D = E/m}$$



Burn the tumor ? Dose will increase its **temperature** !

$$\boldsymbol{E = C_P \times m \times \Delta T}$$

What about the dose ?

$D = E/m$ and $E = C_P \times m \times \Delta T$ (C_P specific heat at cst pressure)

$$\Delta T = {}^{D \times m}/_{C_P \times m}$$

$$\Delta T = {}^{D}/_{C_P}$$

Water as an example : C_P is $4180\ J$ per kg per $°C\ (or\ °K)$

Assuming water target : $\boldsymbol{\Delta T \nearrow 1°C \rightarrow D = 4180\ Gy}$

Median lethal dose LD_{50} is 5 Gy (50% probability of dying) whole body irradiation

In radiotherapy, tumor (localized target) is to receive 2 Gray per session, 35 sessions for a total of 70 Gy

Target volume will not burn

but tumor cells will decrease due to strong biological response

The beam properties have to be under close control

Dosimetry : measurement of the amount of radiation absorbed by a target

Farmer® Chamber
Type 30010

Classical therapy chamber for absolute dosimetry in high-energy photon, electron and proton beams

Features

- Fully guarded chamber
- Sensitive volume 0.6 cm^3, vented to air
- Acrylic wall, graphited
- Aluminum central electrode
- Radioactive check device (option)

The 30010 Farmer chamber is a wide spread ionization chamber for absolute dose measurements in radiation therapy. Correction factors needed to determine absorbed dose to water or air kerma are published in the pertinent dosimetry protocols. The acrylic chamber wall ensures the ruggedness of the chamber. The chamber is designed for the use in solid state phantoms and therefore not waterproof.

Specification

Type of product	vented cylindrical ionization chamber acc. IEC 60731
Application	absolute dosimetry in radiotherapy beams
Measuring quantities	absorbed dose to water, air kerma, exposure
Reference radiation quality	^{60}Co

Materials and measures:

Wall of sensitive volume	0.335 mm PMMA, 1.19 g/cm^3 0.09 mm graphite, 1.85 g/cm^3
Total wall area density	56.5 mg/cm^2
Dimension of sensitive volume	radius 3.05 mm length 23.0 mm
Central electrode	Al 99.98, diameter 1.15 mm
Build-up cap	PMMA, thickness 4.55 mm

Ion collection efficiency at nominal voltage:

Ion collection time	140 µs
Max. dose rate for ≥ 99.5 % saturation ≥ 99.0 % saturation	 5 Gy/s 10 Gy/s
Max. dose per pulse for ≥ 99.5 % saturation ≥ 99.0 % saturation	 0.46 mGy 0.91 mGy

Useful ranges:

Chamber voltage	± (100 ... 400) V
Radiation quality	30 kV ... 50 MV photons (10 ... 45) MeV electrons (50 ... 270) MeV protons
Field size	(5 x 5) cm^2 ... (40 x 40) cm^2

Roos® Chamber

Type 34001

Waterproof plane parallel chamber for absolute dosimetry in high-energy electron and proton beams

Features

- Perturbation-free, minimized polarity effect
- Waterproof, wide guard ring design
- Sensitive volume 0.35 cm^3, vented to air
- Radioactive check device (option)

The 34001 Roos chamber is the golden standard for absolute dose measurements in high-energy electron beams. Modern dosimetry protocols refer to the chamber's design and provide dosimetric correction factors. Its waterproof design allows the chamber to be used in water or in solid state phantoms. The Roos chamber is also well suited for the measurement of high-energy photon depth dose curves. The chamber can be used for dose measurements of proton beams.

Specification

Type of product	vented plane parallel ionization chamber acc. IEC 60731
Application	absolute dosimetry in high-energy electron and proton beams
Measuring quantity	absorbed dose to water
Reference radiation quality	^{60}Co

Materials and measures:

Entrance window	1.01 mm PMMA, 1.19 g/cm^3 0.02 mm graphite, 0.82 g/cm^3 0.1 mm varnish, 1.19 g/cm^3
Total window area density	132 mg/cm^2
Water-equivalent window thickness	1.3 mm
Sensitive volume	radius 7.8 mm depth 2 mm
Guard ring width	4 mm

Ion collection efficiency at nominal voltage:

Ion collection time	125 µs
Max. dose rate for ≥ 99.5 % saturation ≥ 99.0 % saturation	 5.2 Gy/s 10.4 Gy/s
Max. dose per pulse for ≥ 99.5 % saturation ≥ 99.0 % saturation	 0.46 mGy 0.93 mGy

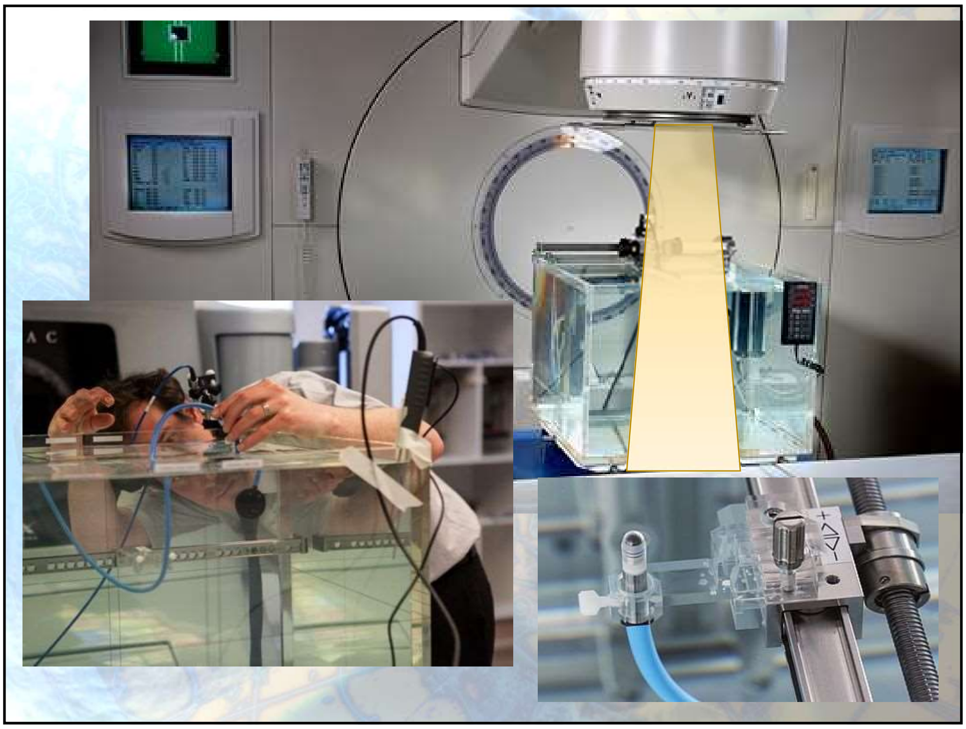
Useful ranges:

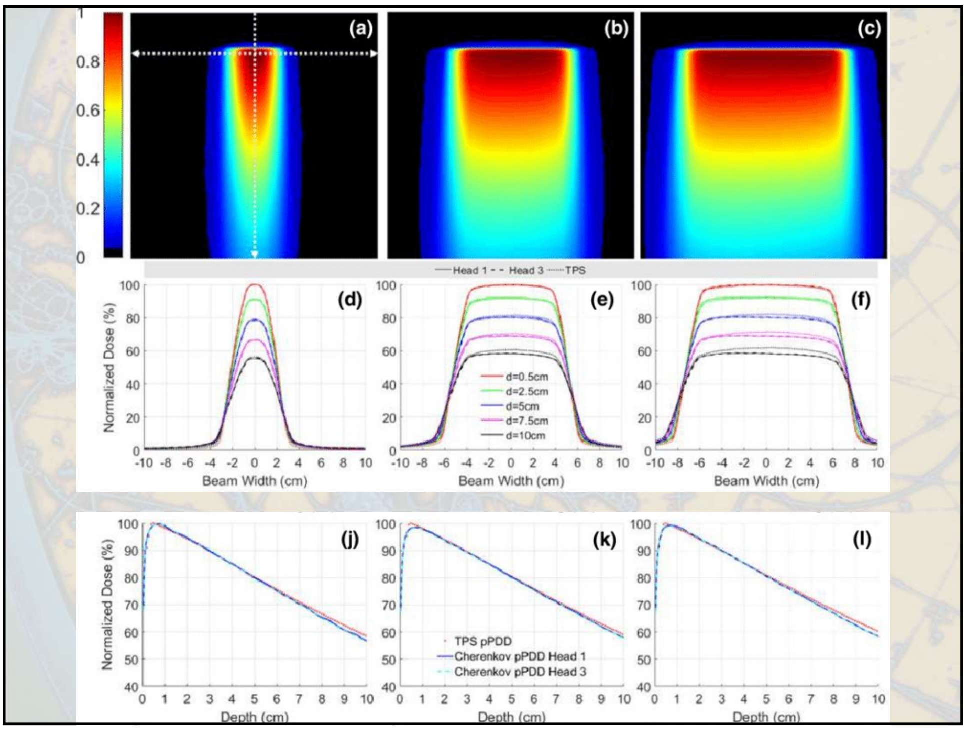
Chamber voltage	± (50 ... 300) V
Radiation quality	(2 ... 45) MeV electrons ^{60}Co ... 25 MV photons (50 ... 270) MeV protons

A water phantom

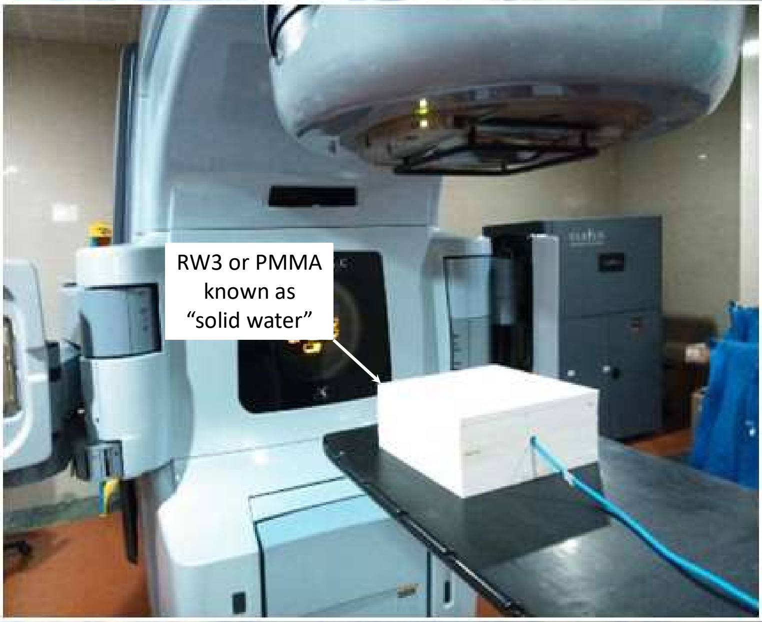
Human body is often considered as water.

A phantom will respond in a similar manner to irradiation, giving access to measurements of dose in 3D



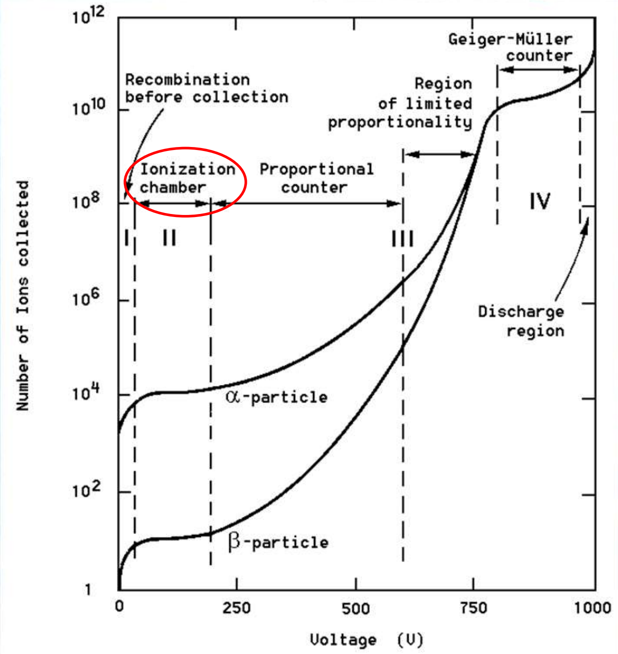

(a)
(b)
(c)
1
0.8
0.6
0.4
0.2
0
Head 1 - - Head 3 TPS
(d)
(e)
(f)
Normalized Dose (%)
Beam Width (cm)
d=0.5cm
d=2.5cm
d=5cm
d=7.5cm
d=10cm
(j)
(k)
(l)
TPS pPDD
Cherenkov pPDD Head 1
Cherenkov pPDD Head 3
Depth (cm)

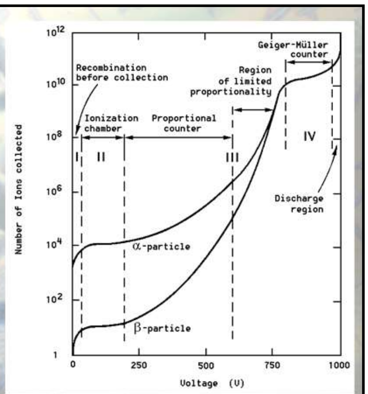
A solid state phantom



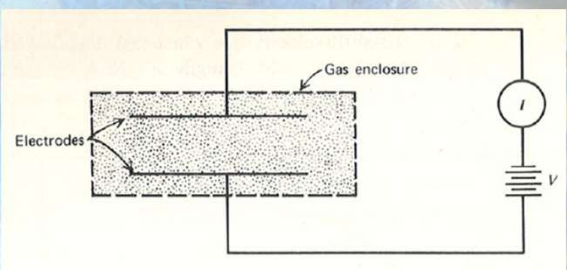
Ionization Chambers,
how do they work ?

You’ve seen that some weeks ago…

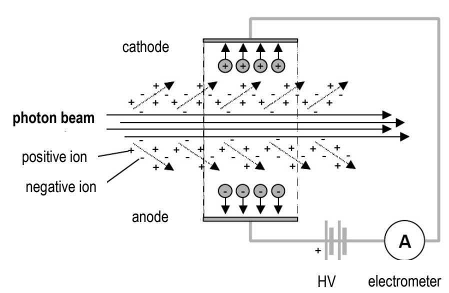




Ionization chamber : volume of air enclosed between 2 polarized electrodes



The ionization chamber



Photons interacts with air molecules :

- photoelectric effect,
- Compton scattering,
- pair creation

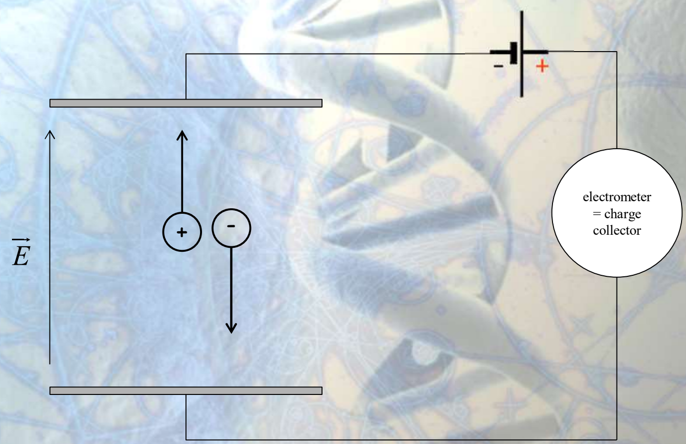
Fast primary electrons (positrons) : air ionization
→ positive ions and slow electrons

Ionization proportional to the energy deposited by the beam

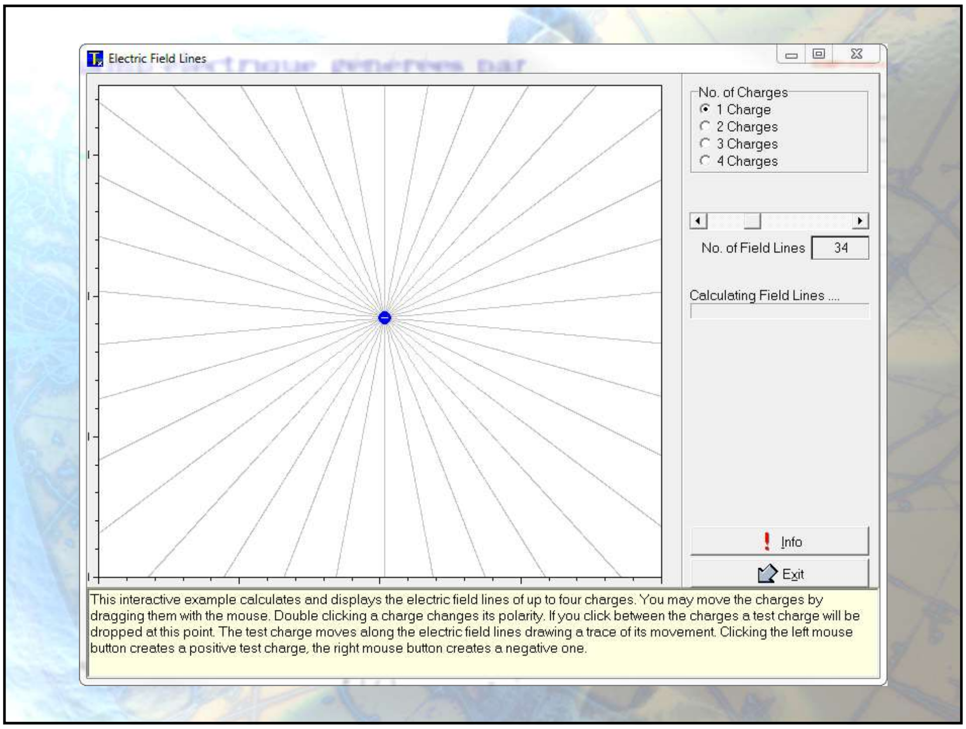
Slow electrons are captured by electronegative molecules ($N_2, O_2, H_2O, \ldots$) or by ion^+

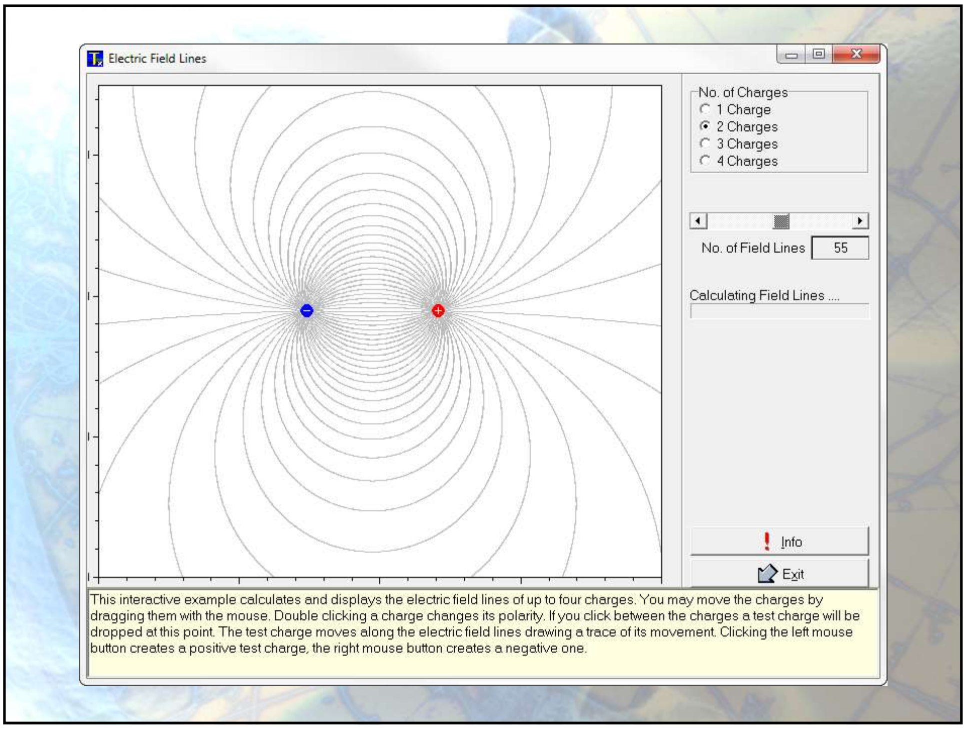
Mainly $\boldsymbol{ion^-}$ and $\boldsymbol{ion^+}$ in the sensitive volume

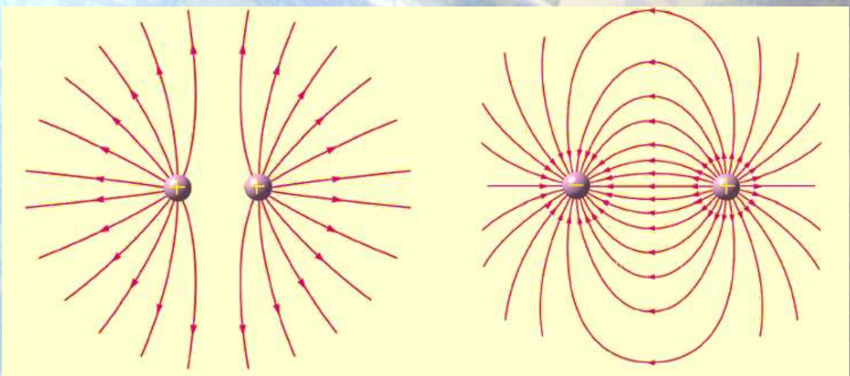
Ions drift towards the electrodes along the electrical field lines : **signal** is collected with a charge collector device (=**electrometer**)



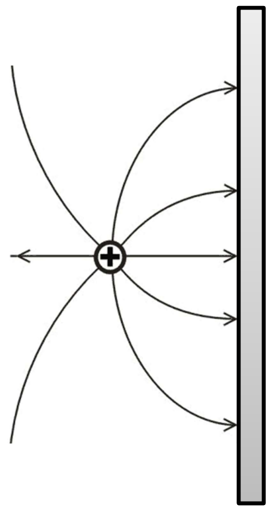
What physical process is responsible for the signal in the electrometer ?


Electric Field Lines
No. of Charges
1 Charge
2 Charges
3 Charges
4 Charges
No. of Field Lines 34
Calculating Field Lines ....
Info
Exit
This interactive example calculates and displays the electric field lines of up to four charges. You may move the charges by dragging them with the mouse. Double clicking a charge changes its polarity. If you click between the charges a test charge will be dropped at this point. The test charge moves along the electric field lines drawing a trace of its movement. Clicking the left mouse button creates a positive test charge, the right mouse button creates a negative one.

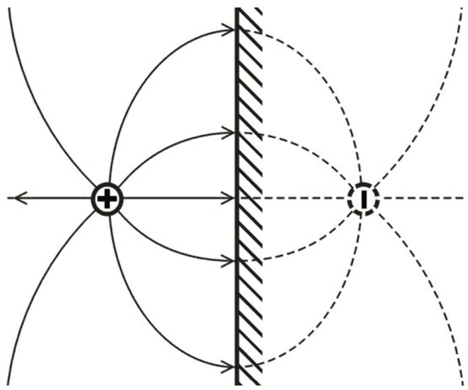

Electric Field Lines
No. of Charges
1 Charge
2 Charges
3 Charges
4 Charges
No. of Field Lines 55
Calculating Field Lines ....
Info
Exit
This interactive example calculates and displays the electric field lines of up to four charges. You may move the charges by dragging them with the mouse. Double clicking a charge changes its polarity. If you click between the charges a test charge will be dropped at this point. The test charge moves along the electric field lines drawing a trace of its movement. Clicking the left mouse button creates a positive test charge, the right mouse button creates a negative one.

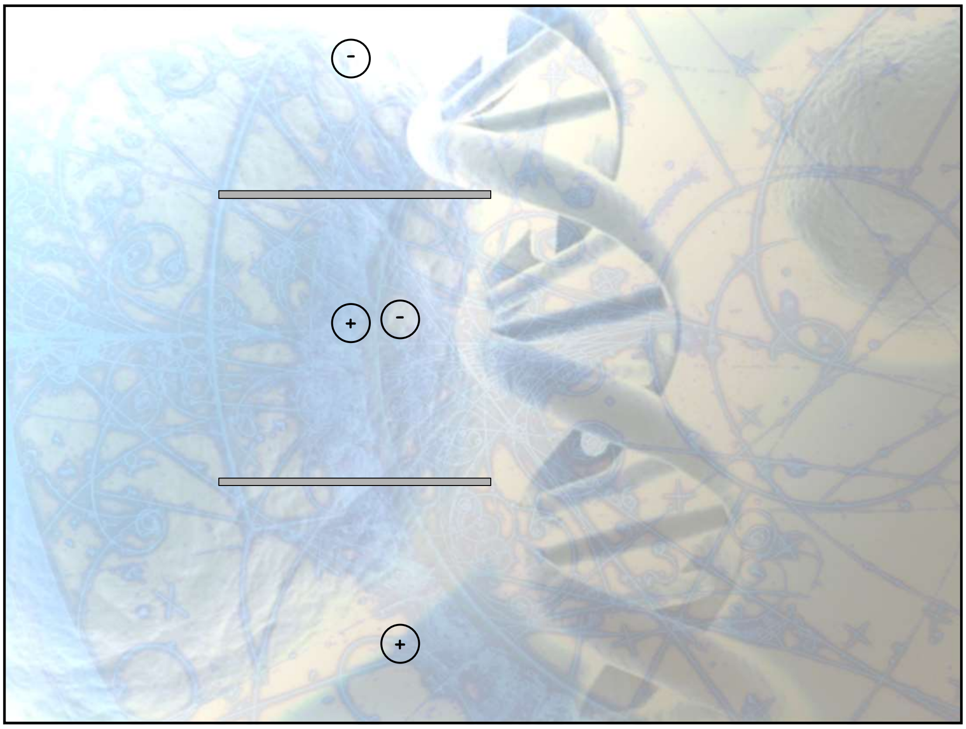


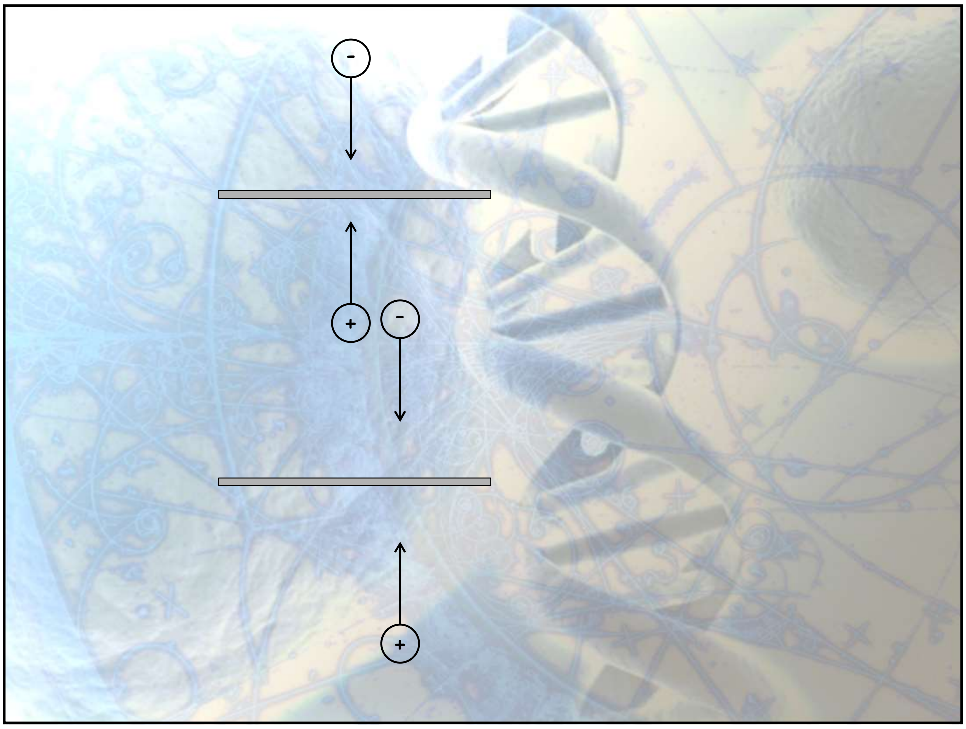
Electromagnetism : Field lines from a single charge above a conductive plane …

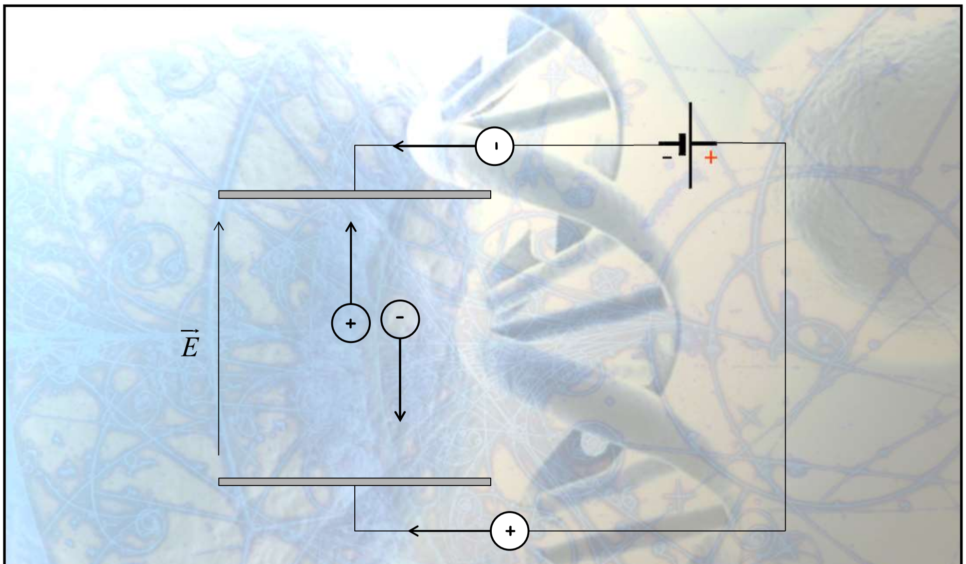


… are the same as the field lines from a pair of opposite charges

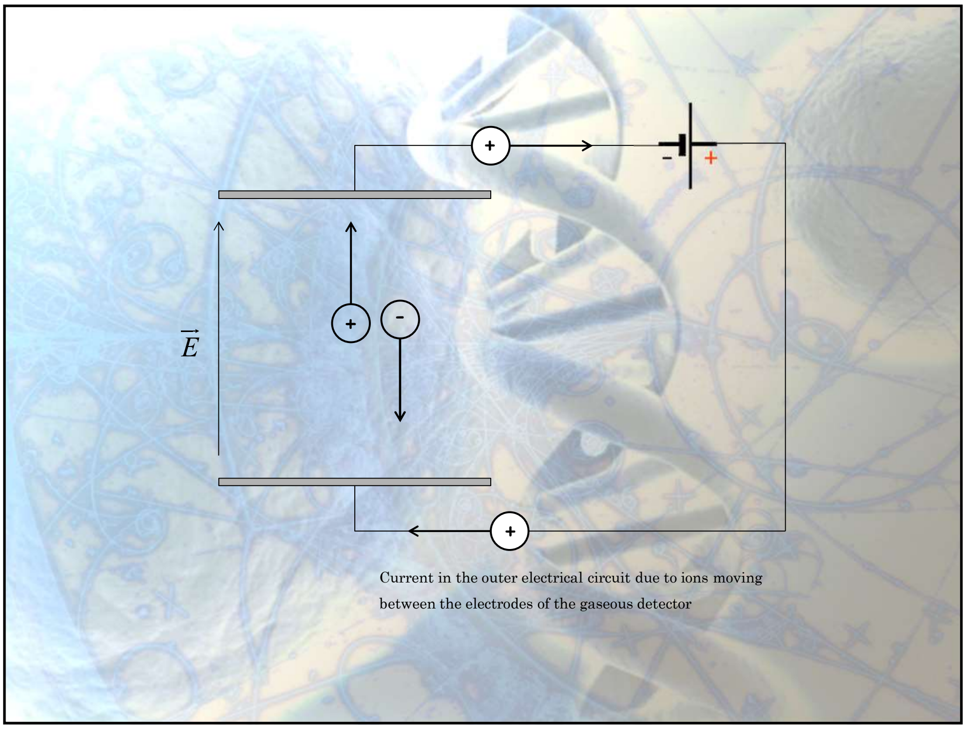


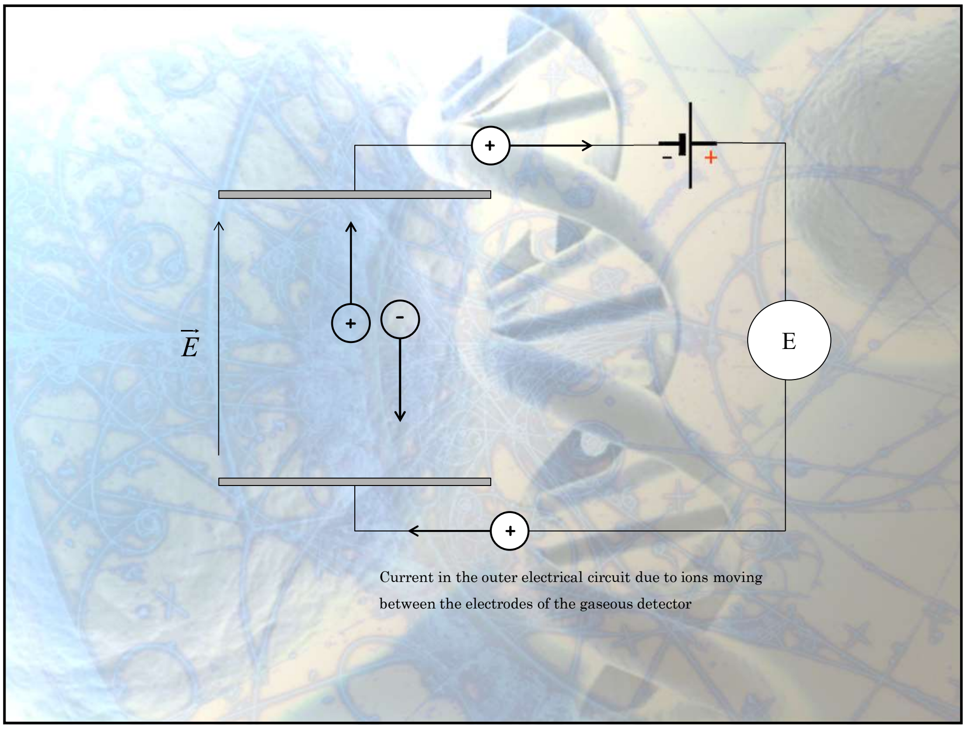


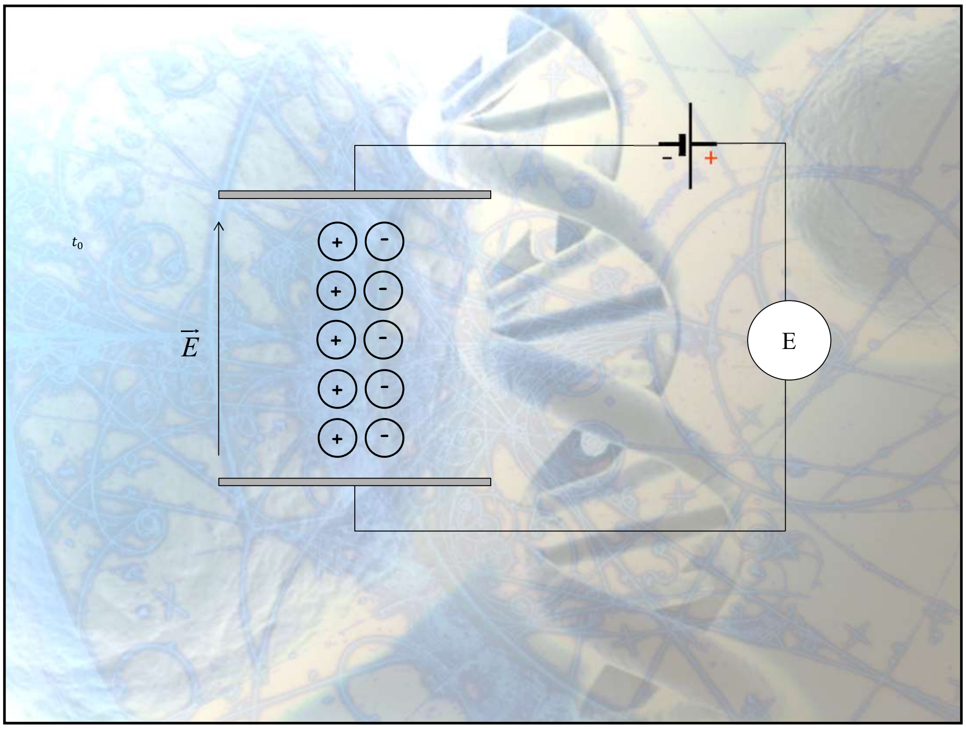




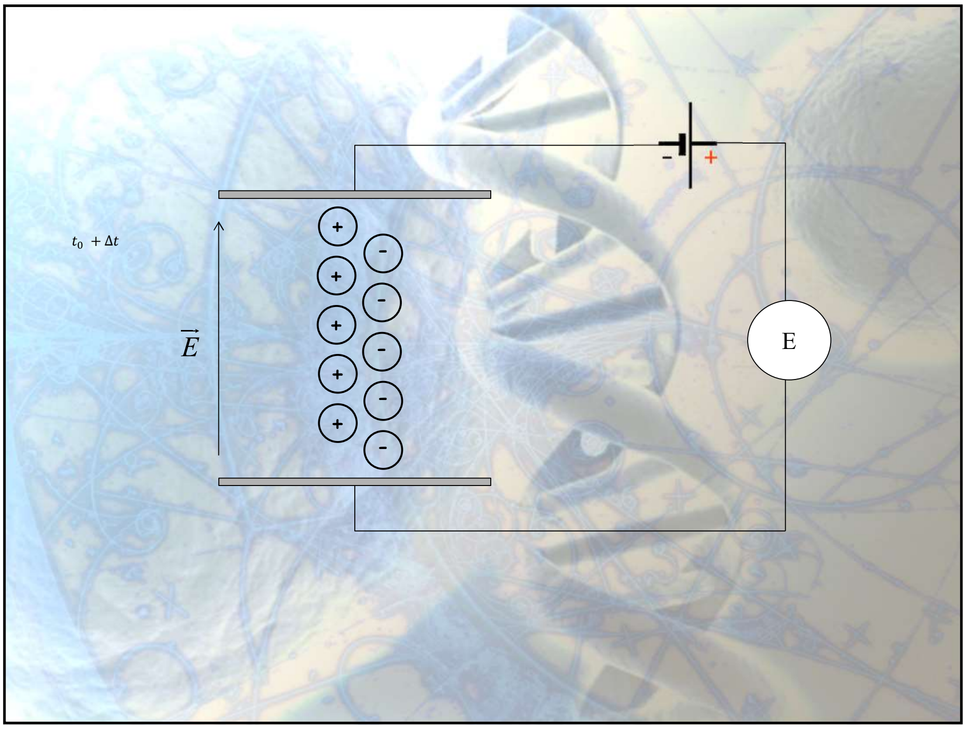
Current in the outer electrical circuit due to ions moving between the electrodes of the gaseous detector


+
-
+
+
-
$\vec{E}$
+
Current in the outer electrical circuit due to ions moving between the electrodes of the gaseous detector

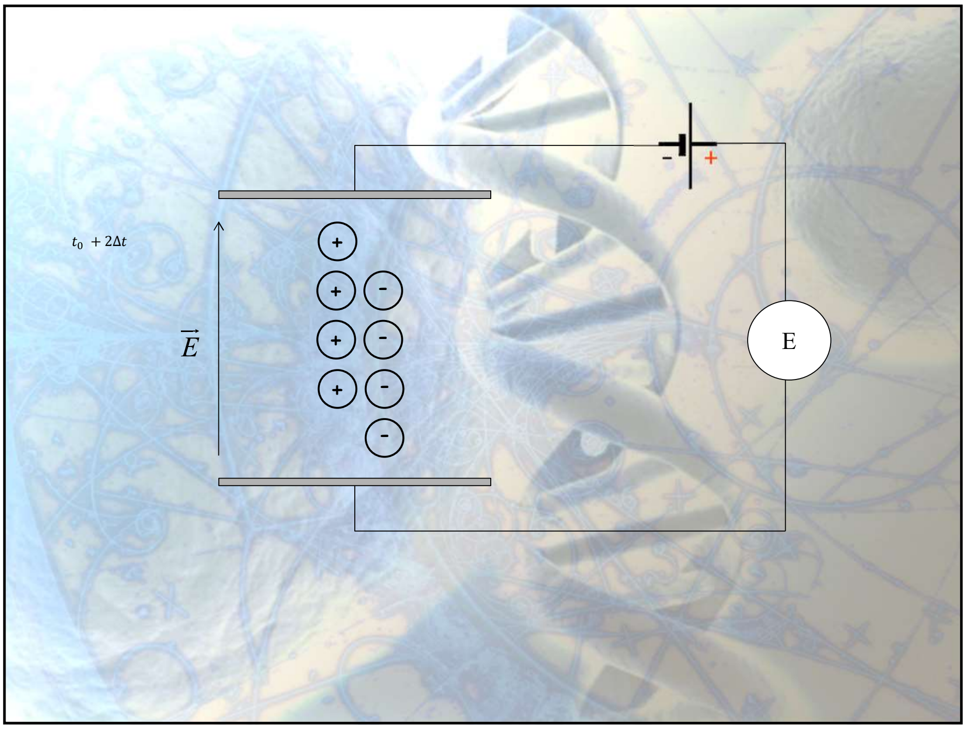

+
-
+
+
-
$\vec{E}$
E
+
Current in the outer electrical circuit due to ions moving between the electrodes of the gaseous detector

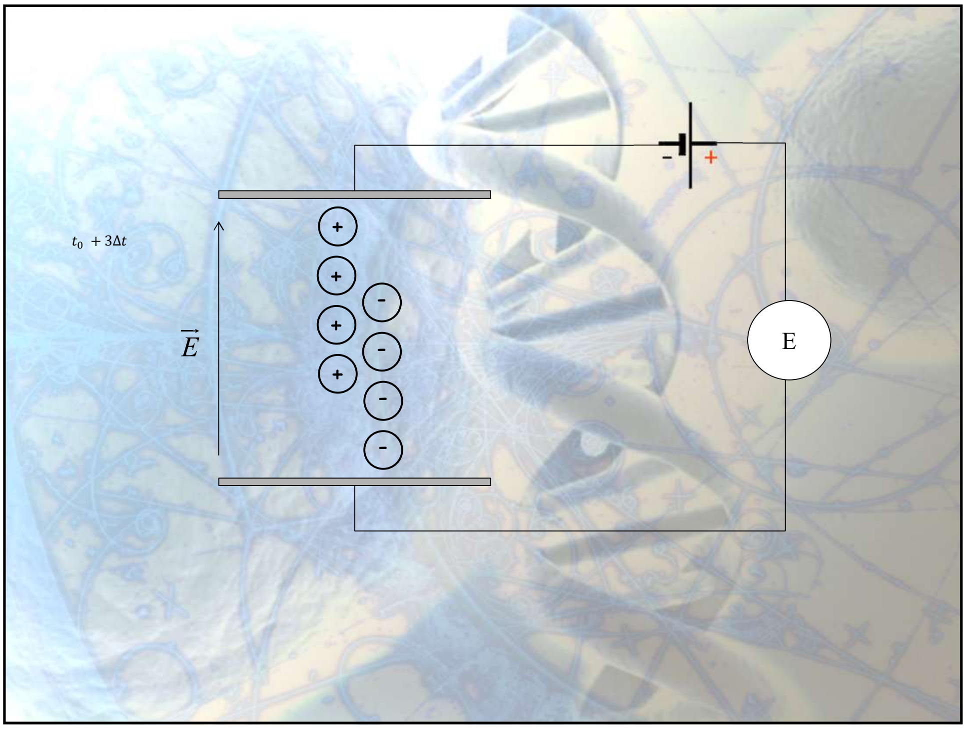


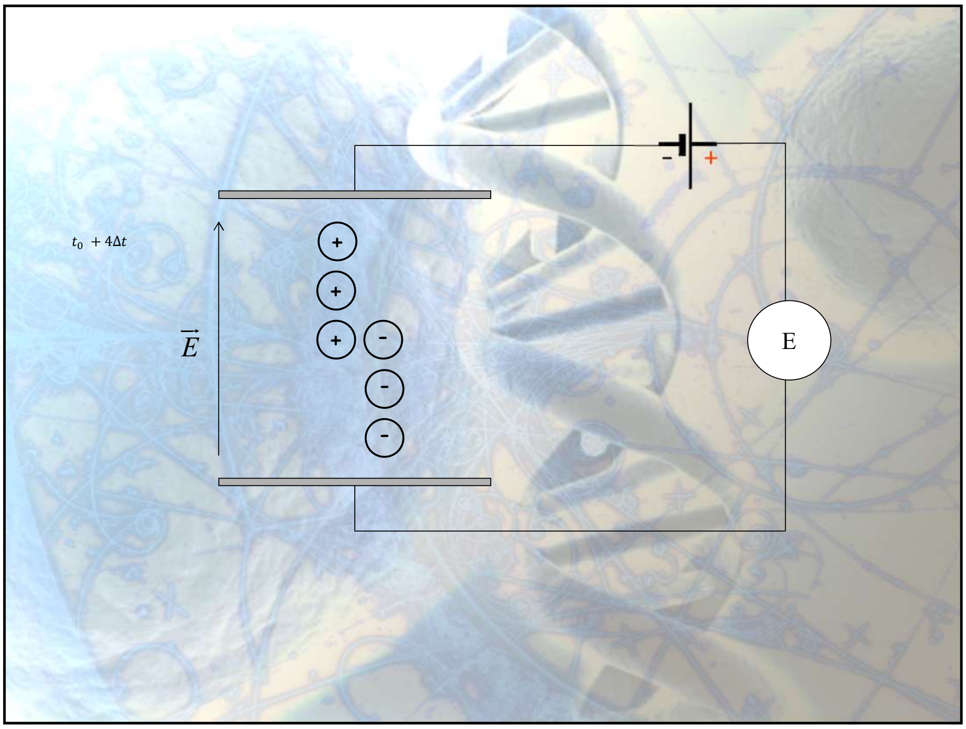
t_0
$\vec{E}$
E
-
+



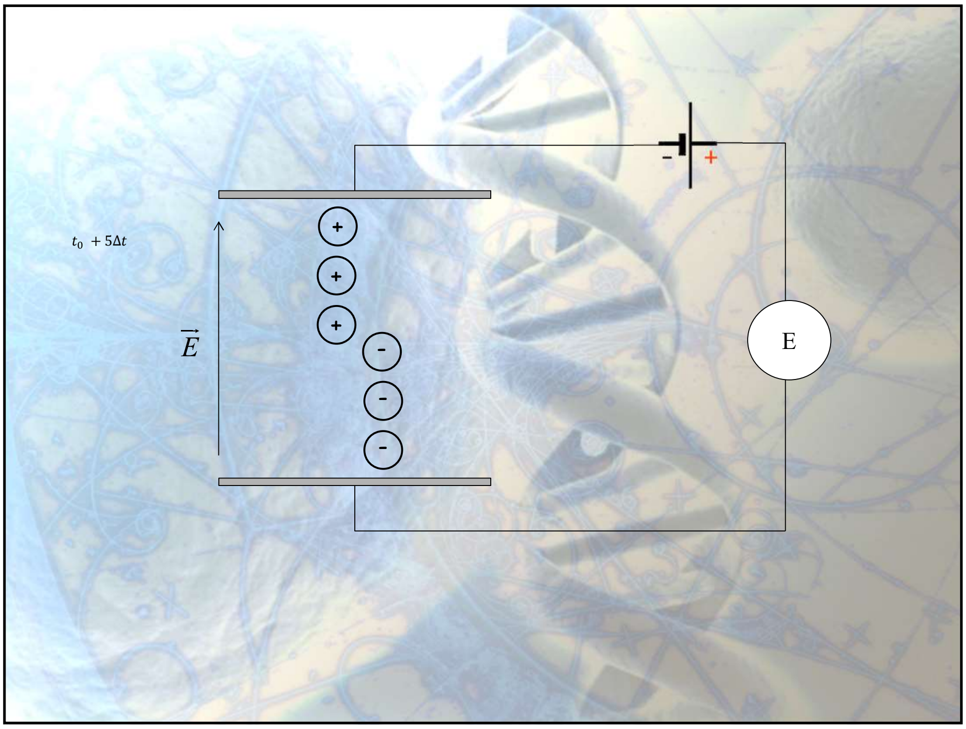
$t_0 + \Delta t$
$\vec{E}$
E
-
+


$t_0 + 2\Delta t$
$\vec{E}$
E

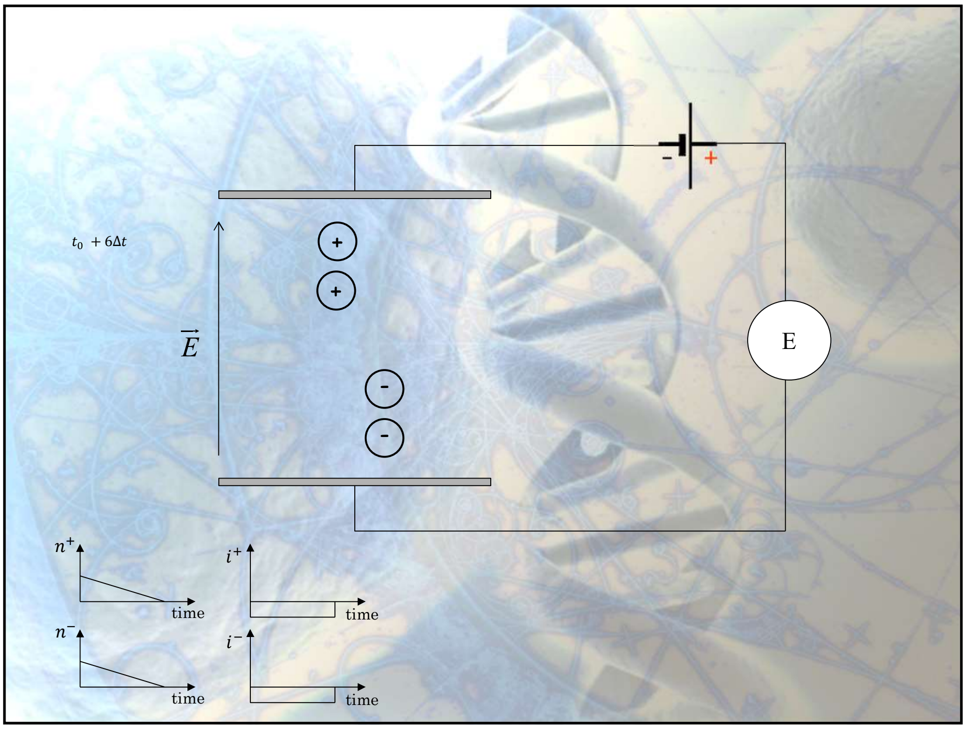

$t_0 + 3\Delta t$
$\vec{E}$
E



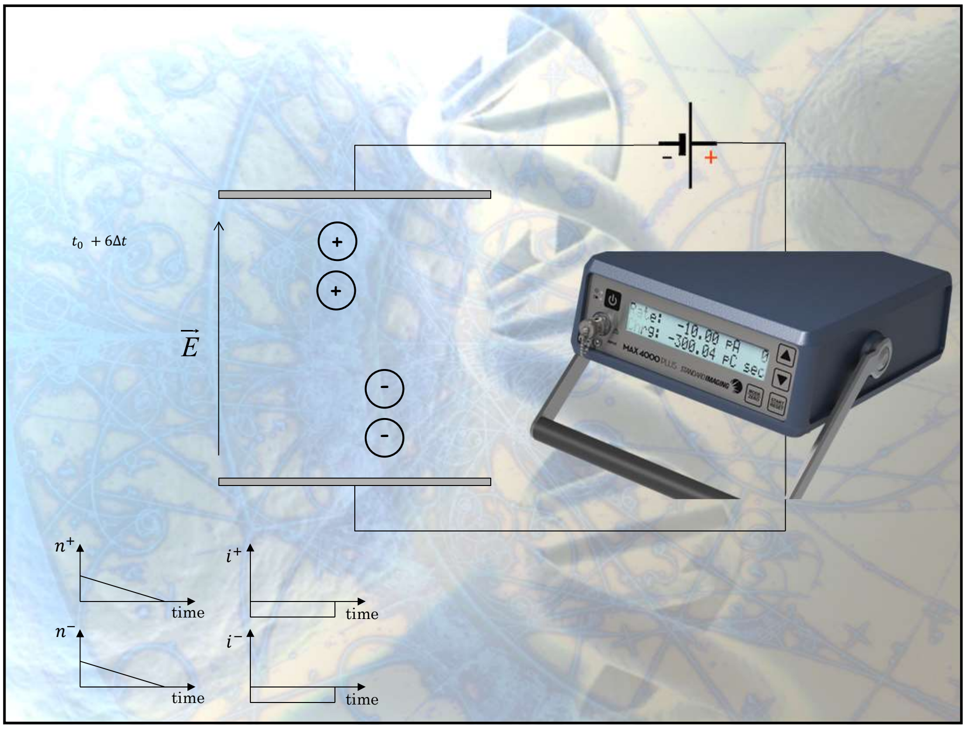
$t_0 + 4\Delta t$
$\vec{E}$
E



$t_0 + 5\Delta t$
$\vec{E}$
E



$t_0 + 6\Delta t$
$\vec{E}$
E
n^+
n^-
i^+
i^-
time
time
time
time

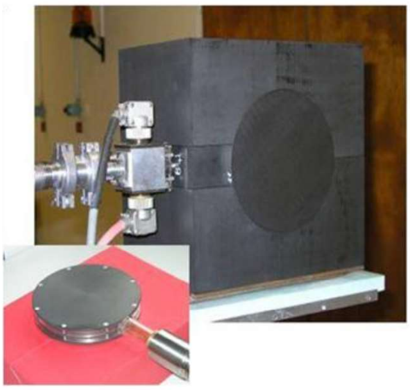


$t_0 + 6\Delta t$
$\vec{E}$
n^+
n^-
i^+
i^-
time
time
time
time
MAX 4000 PLUS

Ionization chamber calibration : from Coulomb to Gray

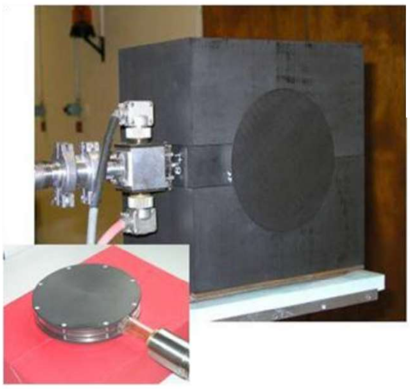
How many Gray corresponds to 1000 pC ?

Calibration with calorimetry



Graphite calorimeter : all the energy from the beam interaction is converted into heat

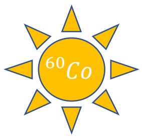
Calibration with calorimetry

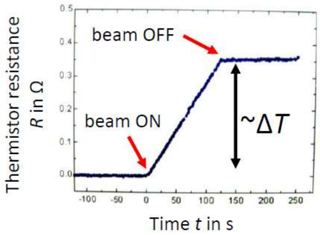


Energy in the graphite calorimeter :

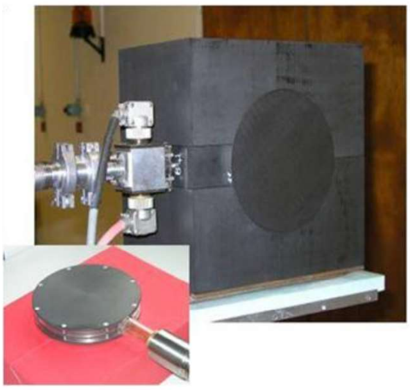
temperature ↗ $E = C_P \times m \times \Delta T$

$$E = \int_{t_{start}}^{t_{end}} a(t) \times \frac{\Omega}{4\pi} \times \cdots \times dt$$



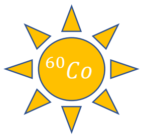


Calibration with calorimetry



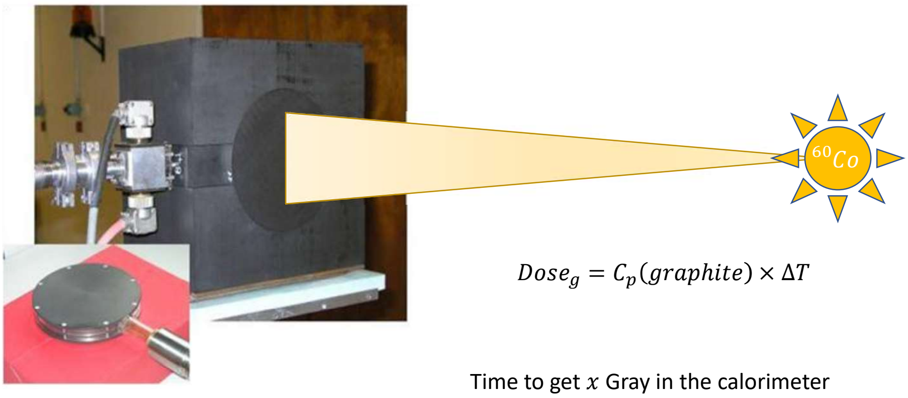
$E = C_P \times m \times \Delta T$

$$E = \int_{t_{start}}^{t_{end}} a(t) \times \frac{\Omega}{4\pi} \times \cdots \times dt$$



$$Dose_g = C_p(graphite) \times \Delta T$$

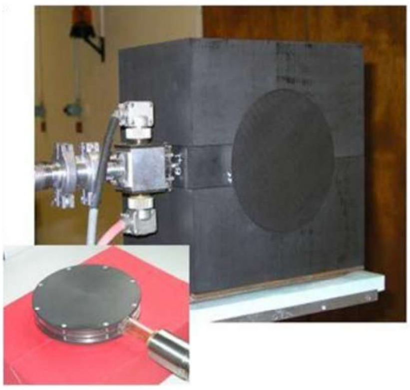
Calibration with calorimetry

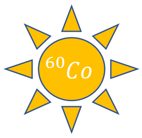


$$Dose_g = C_p(graphite) \times \Delta T$$

Time to get x Gray in the calorimeter

Calibration with calorimetry

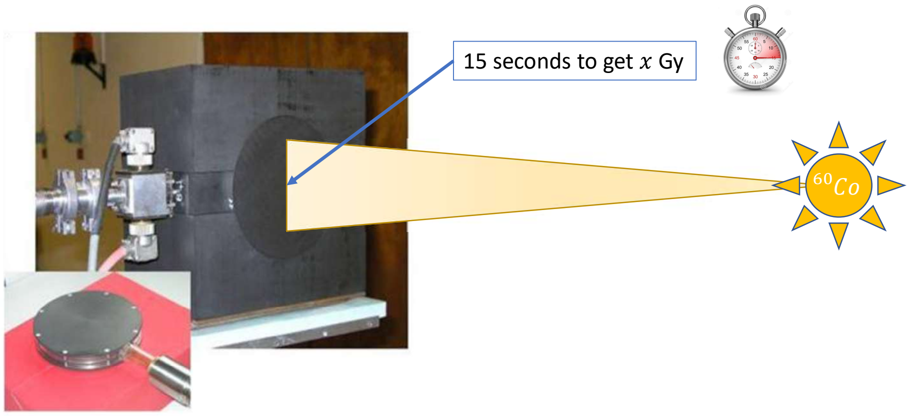




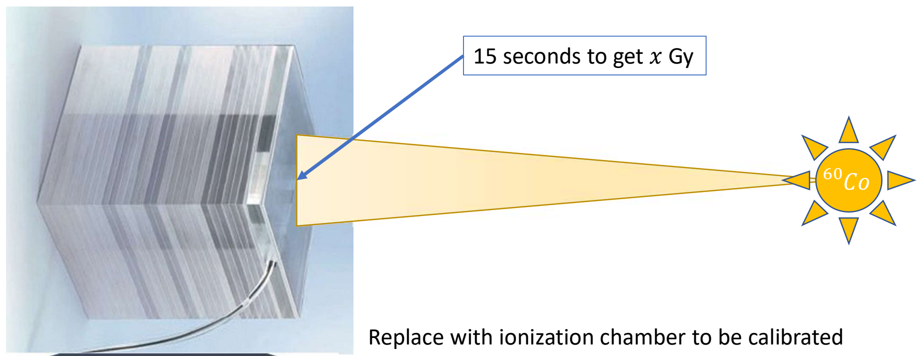
$$Dose_g = C_p(graphite) \times \Delta T$$

Time to get x Gray in the calorimeter

Calibration with calorimetry



Calibration with calorimetry



Replace with ionization chamber to be calibrated

Irradiate for 15 seconds

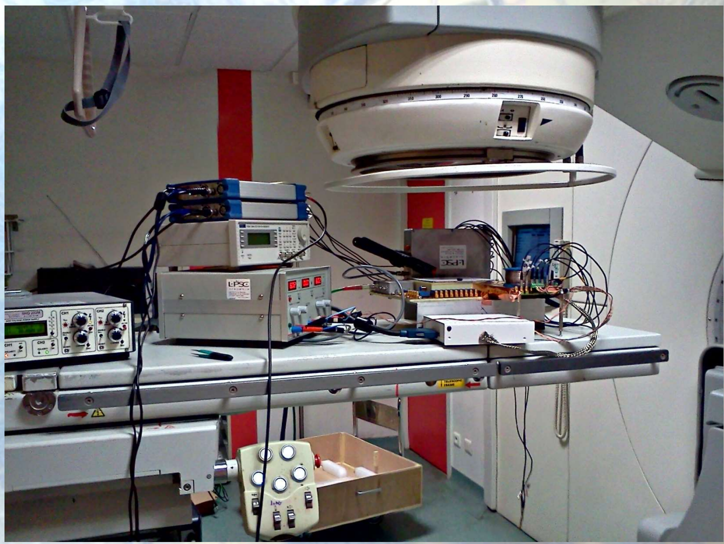
Read the accumulated charge

Apply correction factors and Compute the calibration coefficient to Gray from Coulomb

Ionization chamber calibration : from Coulomb to Gray

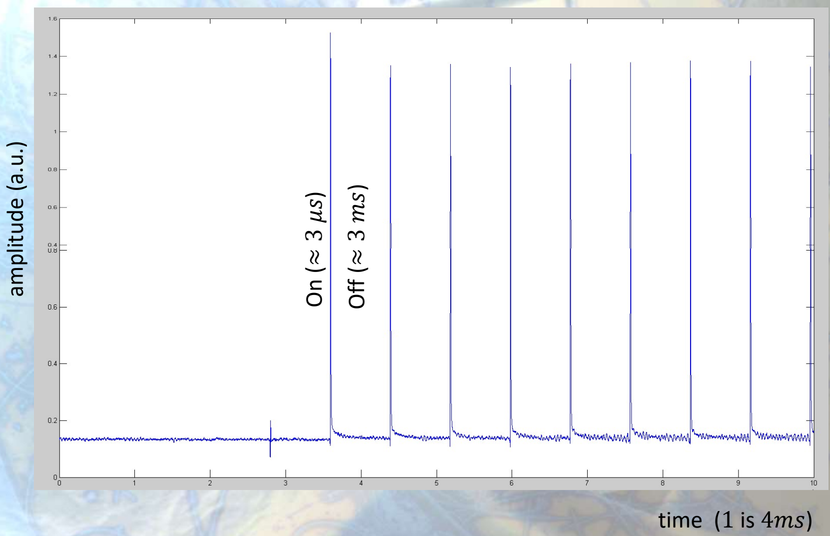
Ionization chamber calibration : from Coulomb to Gray

Grenoble Public Hospital in the evening …
… a bunch a physicists in the radiotherapy treatment room with their equipment

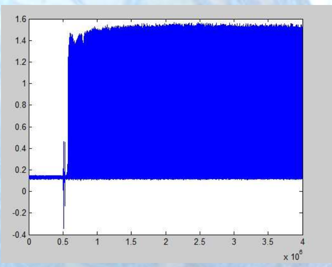


Readout : IC + amplifier ($I \rightarrow V$) + recorder in real time

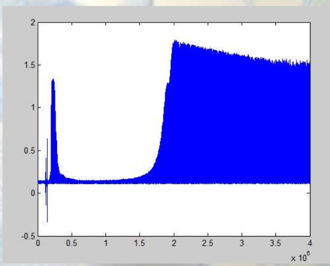
… Linac provides **pulses** until the right dose is delivered …



Zooming out : are the pulses constant over time ?

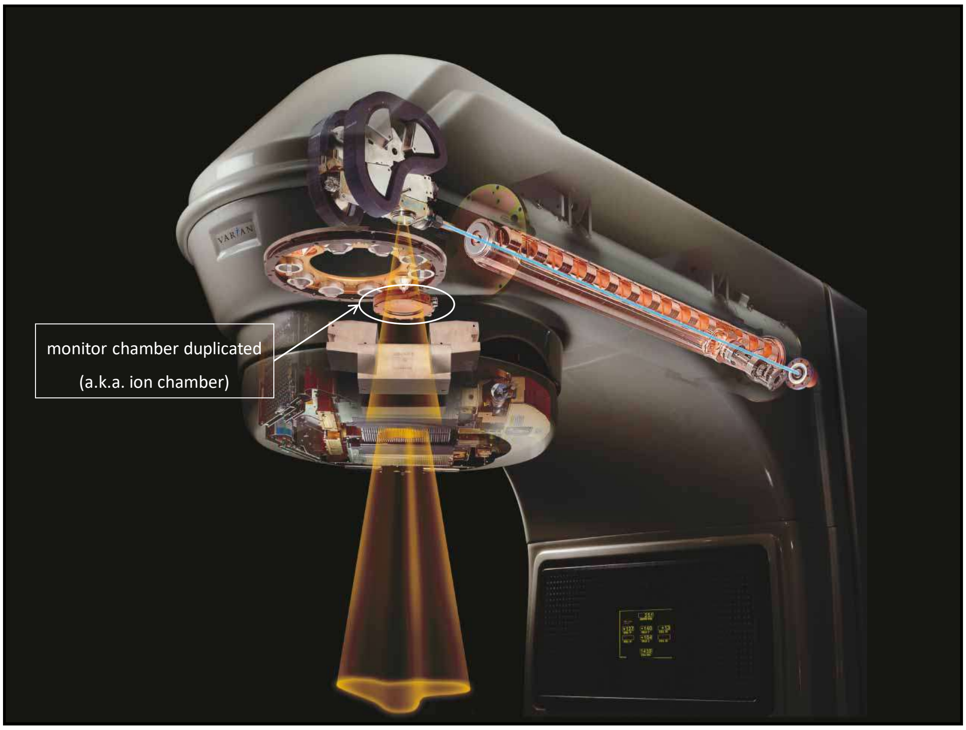


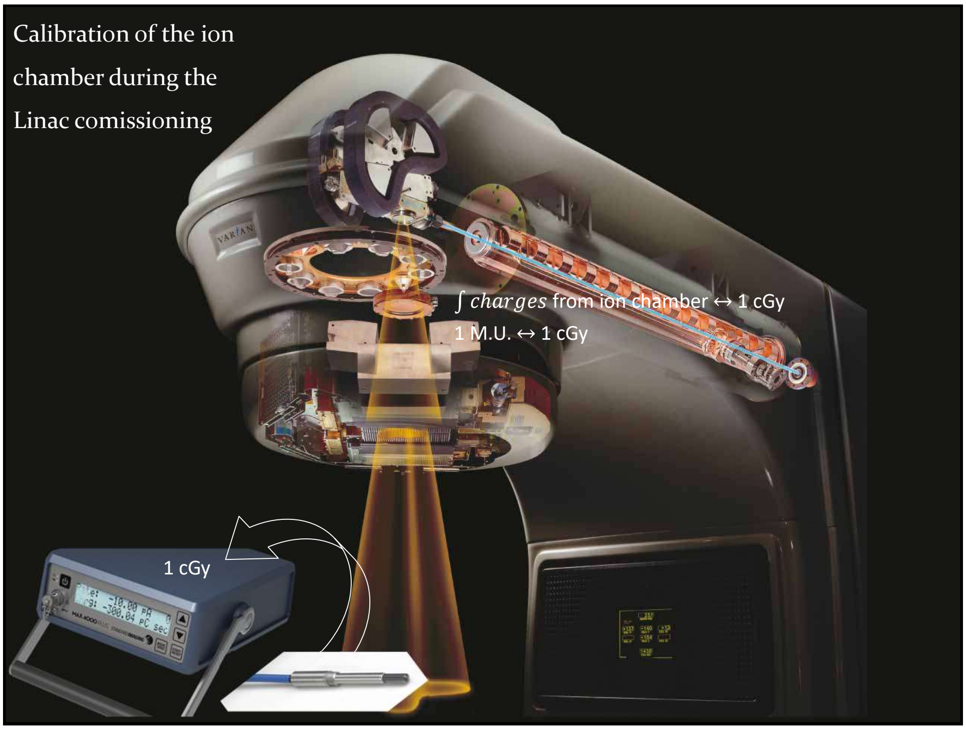
1st acquisition : pulses quickly reaches a stable intensity →

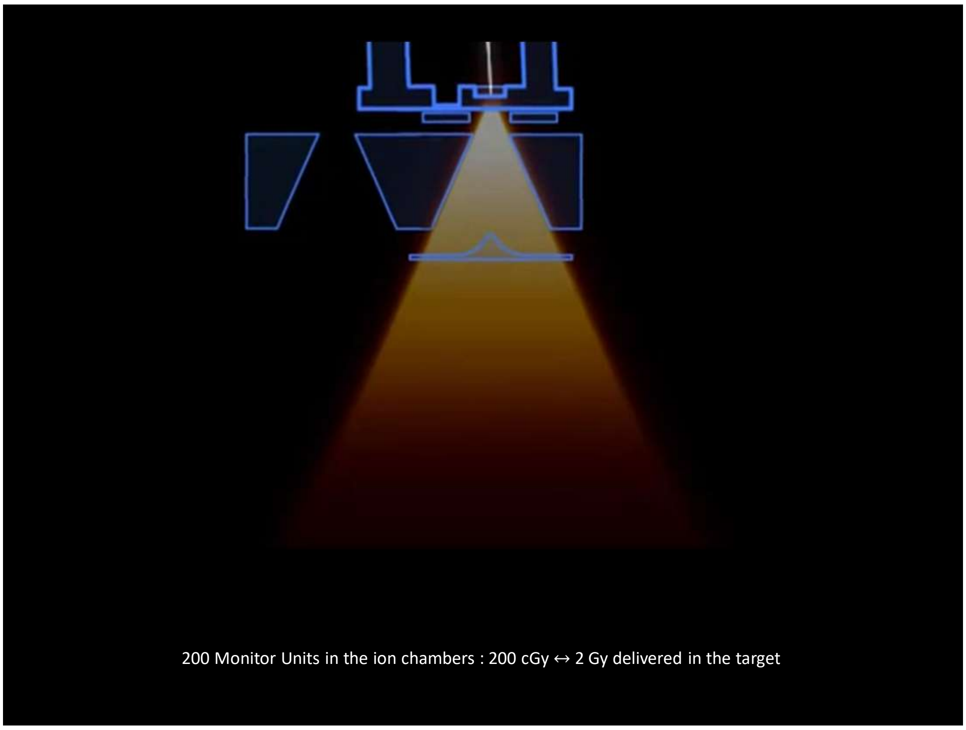


2nd acquisition : beam starts, intensity ↗ but ↘ quikly.
After some time, intensity increases to recover from lost pulses, before reaching a stable plateau

Linac : treatment delivery needs **constant beam properties monitoring in real time**


monitor chamber duplicated
(a.k.a. ion chamber)


Calibration of the ion chamber during the Linac comissioning
$\int charges$ from ion chamber ↔ 1 cGy
1 M.U. ↔ 1 cGy
1 cGy


200 Monitor Units in the ion chambers : 200 cGy ↔ 2 Gy delivered in the target

End of 1st part

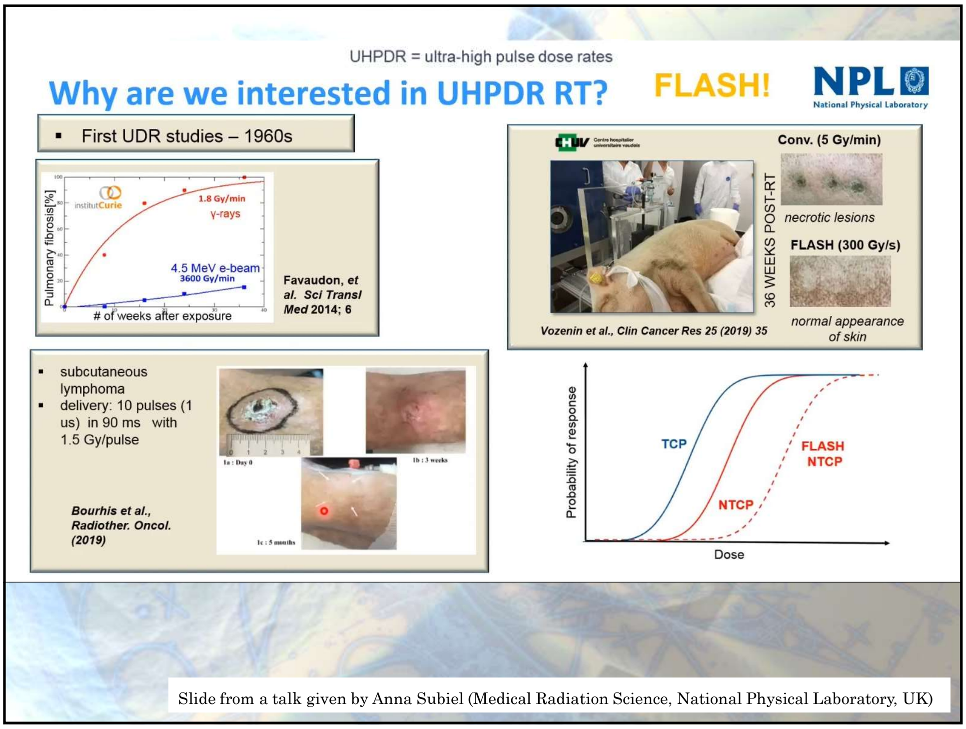
Beam monitoring in radiotherapy

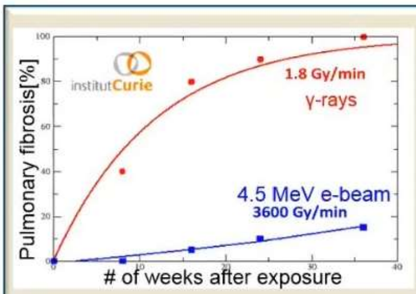
Everything was oversimplified,
many approximations,
many borderline explanations
but you should have a feeling of the overall picture

Radiotherapy : Beam monitoring in high-intensity radiotherapy treatments beams …

… is still under study and people are working on it !


Very High Energy Electron Radiotherapy Workshop (VHEE'2020)
5-7 October 2020
CERN
Europe/Zurich timezone
Search...
VHEE2020
5-7 October 2020
Cherenkov in water
Exit Window
Water phantom
Radiosensitive films
YAG screen
Charge monitor
Quadrupole
Camera


UHPDR = ultra-high pulse dose rates
Why are we interested in UHPDR RT?
FLASH!
NPL
National Physical Laboratory
First UDR studies – 1960s
Pulmonary fibrosis[%]
1.8 Gy/min
γ-rays
4.5 MeV e-beam
3600 Gy/min
# of weeks after exposure
Favaudon, et al. Sci Transl Med 2014; 6
Conv. (5 Gy/min)
necrotic lesions
FLASH (300 Gy/s)
normal appearance of skin
36 WEEKS POST-RT
Vozenin et al., Clin Cancer Res 25 (2019) 35
subcutaneous lymphoma
delivery: 10 pulses (1 us) in 90 ms with 1.5 Gy/pulse
Bourhis et al., Radiother. Oncol. (2019)
Probability of response
TCP
NTCP
FLASH NTCP
Dose
Slide from a talk given by Anna Subiel (Medical Radiation Science, National Physical Laboratory, UK)



Favaudon, *et al. Sci Transl Med* 2014; 6

What Is Pulmonary Fibrosis?

Pulmonary fibrosis is one of a group of lung disorders that cause **scar tissue to form in the lungs**.

Over time, the scarred tissue in the lungs makes it hard to breathe. People with pulmonary fibrosis often feel out of breath and may find it a challenge to do simple physical activities, such as climbing stairs or running errands.

Dosimetric challenges at FLASH

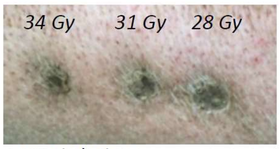
Example: FLASH irradiation of pig skin

Centre hospitalier universitaire vaudois

Conventional and FLASH Irradiation (with same total dose)

36 weeks post-RT

Conventional (5 Gy/min)



necrotic lesions

FLASH (300 Gy/s)

3 Gy/pulse

normal appearance of skin

Vozenin *et al.*, Clin Cancer Res 25 (2019) 35
http://dx.doi.org/10.1158/1078-0432.CCR-17-3375

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Dosimetric challenges at FLASH

Example: Treatment of the first human patient with FLASH-RT

Centre hospitalier universitaire vaudois

Disease:
lymphoma on skin

conventional RT:
20 Gy in 6 - 10 fractions
high grade acute skin reactions
takes >3 months to heal

FLASH-RT:
10 pulses (of 1 μs duration) in 90 ms
with **1.5 Gy/pulse**

Day 0

after 3 weeks

(max. of skin reactions)

after 5 months

Bourhis *et al.*, Radiother. Oncol. (2019)
DOI: 10.1016/j.radonc.2019.06.019

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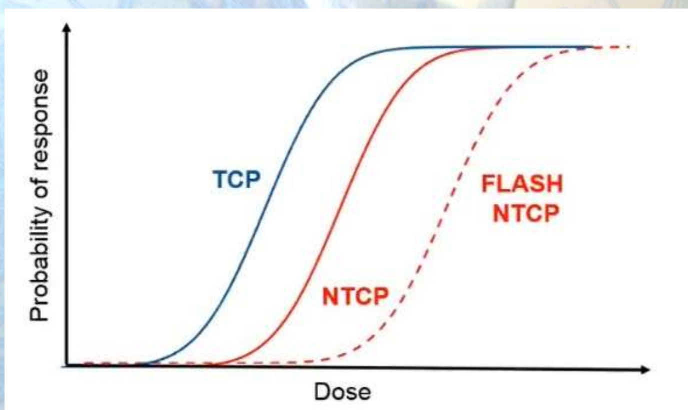
FLASH does look promising !

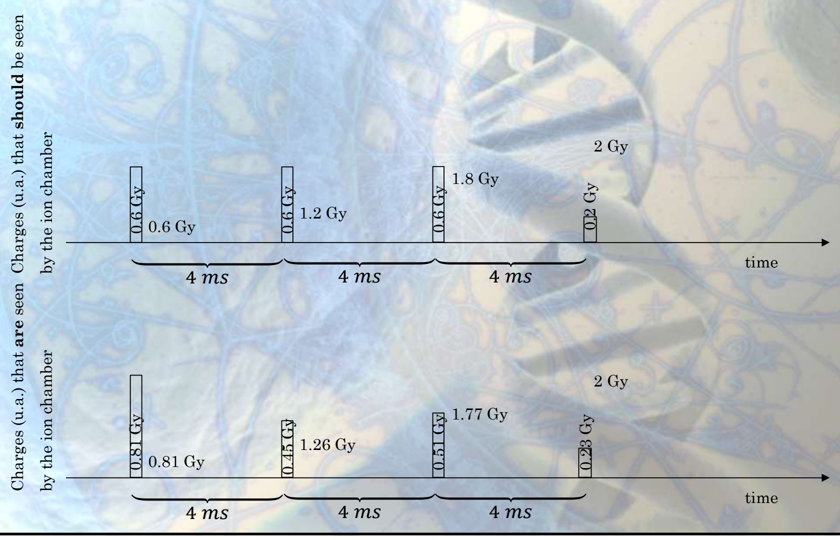


But…

FLASH effect takes with $\dot{D} > 0{,}6\ Gy/pulse$

With very high dose rate, the delivery of 2 Gy takes less than a second

Control in real time of the delivered dose is of paramount importance



High dose-per-pulse electron beam dosimetry: Usability and dose-rate independence of EBT3 Gafchromic films

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Department of Radiation Oncology, Lausanne University Hospital, Lausanne, Switzerland
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(Received 24 June 2016; revised 2 December 2016; accepted for publication 7 December 2016; published 13 February 2017)

1. INTRODUCTION

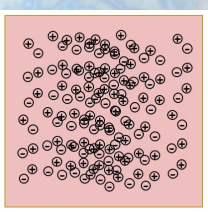
Preclinical studies have shown that irradiations using a high dose-per-pulse electron beam with a high dose rate can increase the differential response between normal and tumor tissue compared to radiotherapy delivered with conventional dose rates (of a few Gy/min).[1] Extremely fast irradiations may also improve motion management issues, since the treatment could be delivered to the patient more rapidly than the timeframe of physiological motions.[2,3] These investigations raised the challenge of performing reliable dosimetry in unusual irradiation conditions, such as those produced by a prototype high dose-per-pulse linac recently installed in our department. Ionization chambers, which are in general the instruments of choice for reference dosimetry, cannot be used directly because of strong saturation effects induced by the intense beam of the prototype linac, which cannot be corrected in a satisfactory way by existing saturation models.[4–6] In this work, we examined the usability of Gafchromic EBT3 films for reference dosimetry in high dose rates/dose-per-

725 Med. Phys. 44 (2), February 2017 0094-2405/2017/44(2)/725/11 725

Recombination processes in the gas

- Columnar recombination (e^{-}, ion^{+}) in column along initial ionizing particle : electrons recombine with their parent ion. Mainly depends on the LET of the ionising particle. Independent on the dose rate

- **Volume recombination** when charges are drifting towards the electrodes. Depends on **irradiation rate** but can be reduced by increasing electrical field between electrodes

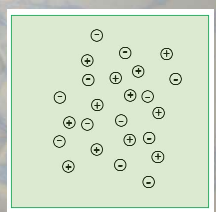


Recombinations in an ion chamber

Definition of a recombination collision rate R ($m^{-3}s^{-1}$) and of a recombination coefficient α ($m^{3}s^{-1}$) such as:

$$R = -\frac{dn^{+}}{dt} = -\frac{dn^{-}}{dt} = \alpha n^{+} n^{-}$$

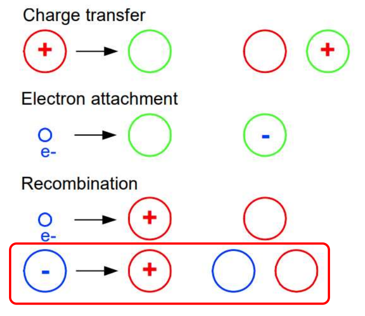
with n^{+} and n^{-}, the volume densities of charge



Recombination can be neglected (apply small corrections factors) in conventional RT

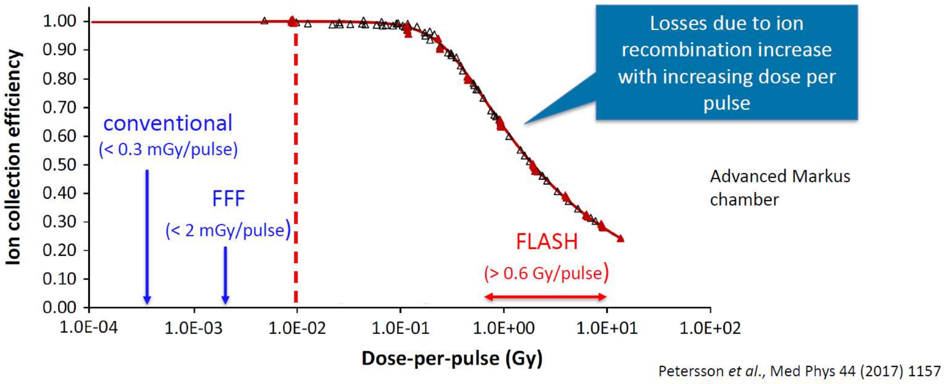
Recombination is a problem in FLASH therapy :

- Some ions are vanishing : fraction of original charge is lost
- **Non linear contribution to final signal**
- **Tricky to compensate for the loss of linearity**



Dosimetric challenges at FLASH

Typical performance of an ionization chamber



Petersson *et al.*, Med Phys 44 (2017) 1157
https://doi.org/10.1002/mp.12111

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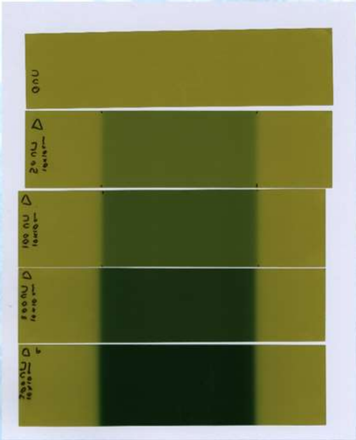
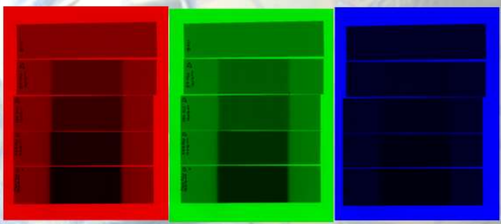
Radiochromic films

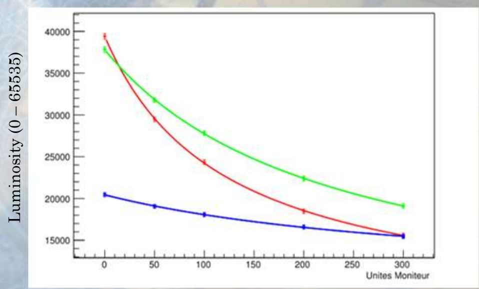


Calibration : increasing dose (or Monitor Units) on each film strip

Wait for at least 6 hours for the change of color to stabilize



Scan strips with a flatbed scanner. Decompose white to RGB



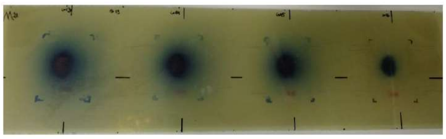
Calibration curves

Dosimetric challenges at VHEE

Verification of energy independence of passive dosimeters at VHEE

requested dose: 20 Gy 15 Gy 10 Gy 1 Gy

151 MeV



irradiated EBT3 film front side

dose range limits

EBT3:
< 40 Gy

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Dosimetric challenges at VHEE

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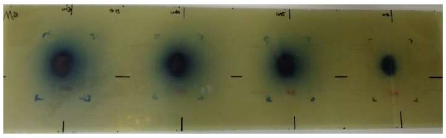

irradiated EBT3 film front side

4 stacks of 4 alanine pellets on the rear face of the EBT3 films

<u>dose range limits</u>

EBT3:
< 40 Gy

PTB Alanine dosimetry system:
< 25 Gy

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Dosimetric challenges at FLASH and VHEE

Crucial point dosimetry

If an error is made in dosimetry, the difference in tissue response between conventional irradiation and ultra-high dose rate irradiation at apparently the same total dose may be due to this error and not due to the FLASH effect.

Tools and methods established in dosimetry for conventional RT are not suitable for FLASH-RT or VHEE-RT

no active dosimeters for real time dosimetry

no formalism (Codes of Practice) for reference dosimetry

no corresponding primary standard

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Ultra High Pulse Dose Rates might be the next step in radiotherapy

Clear reduction of the complications on the normal tissue side

Many things have to be done :

- Define a reference procedure to get a "universal Gray" from UHPDR
- Develop new detectors (dosimeters and ion chambers) to avoid saturation and charge collection loss
- Define procedures to commission UHPDR machines to come