ICTR-PHE 2016

Uniting physics, biology and medicine for better healthcare

Metal implanted multi-functional nanovectors for targeted radiotherapy and diagnostics of cancer

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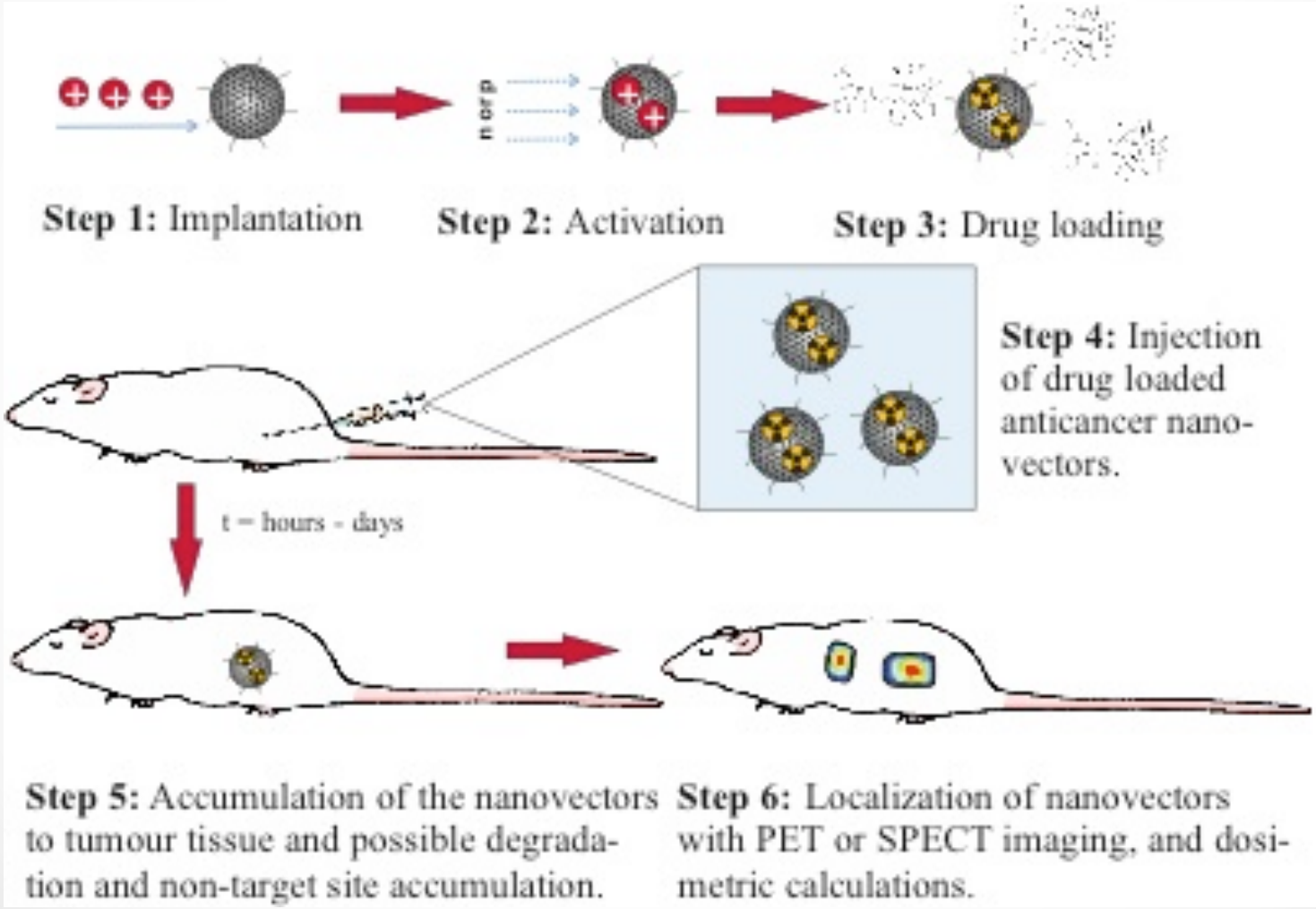
Outline

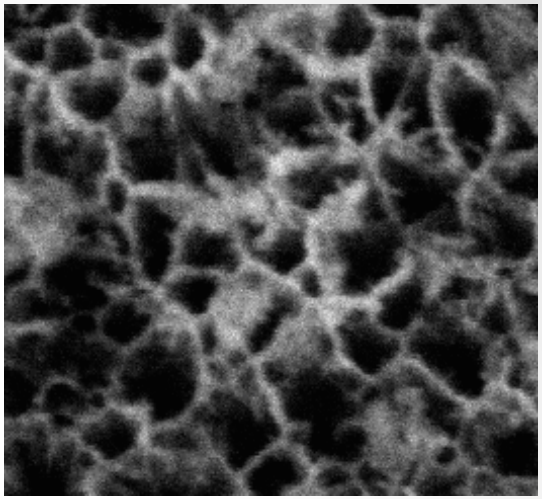
- Principle
- Results on activation experiment
- Results on direct implantation experiment
- Conclusion

Principle

- Radionuclide + mesoporous silicon nanoparticles → targeted radiotherapy



Principle (2) – PSi nanoparticles

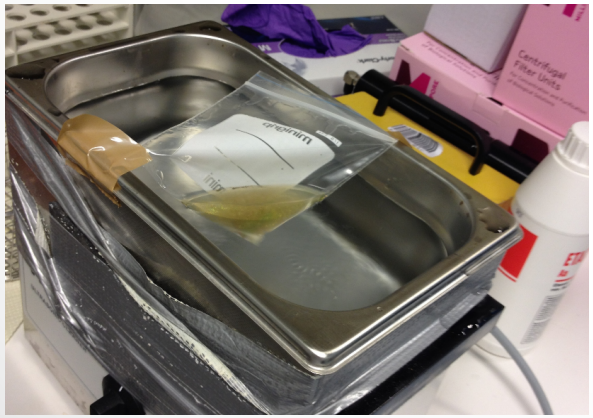


Properties of mesoporous silicon

- biocompatible & biodegradable
- Silicon lattice is amenable for ion implantation
- High temperature resistance
- High adsorption capacity with anti-cancer drug

Particles fabrication

- For activation: The particles have been deposited with copper using electroless deposition technique followed by thermal annealing and carbonization – processed to nanosize particles by pulse-etching
- For direct implantation: sonication of wafers in EtOH in a minigrip bag for several hours



Principle (3) – Radionuclide

- All the selected nuclides have a therapeutic application, either by utilising β^- particles or Auger/conversion electrons. All nuclides have also emissions that can be utilised in PET (^{64}Cu) or SPECT (^{169}Yb).

Nuclide	$T_{1/2}$	Main emissions	Production	Application
^{64}Cu	12.7 h	e^-, E=6.6 keV, I_e=22.5% β^+, E_{max}=653 keV, I_β=17.6% β^-, E_{max}=579 keV, I_β=38.5%	**^{63}Cu(n,γ)**, ^{64}Ni(p,n)	Imaging (PET, autoradiography) Therapeutic
^{169}Yb	32.0 d	e^-, E=5.7 keV, I_e=161.8% e^-, E=6.1 keV, I_e=74.8% e^-, E=7.9 keV, I_e=17.3% e^-, E=41 keV, I_e=10.6% e^-, E=50 keV, I_e=34.3% e^-, E=118 keV, I_e=10.9% e^-, E=139 keV, I_e=12.9% X-ray, E=50 keV, I_γ=52.5% X-ray, E=51 keV, I_γ=91.6% X-ray, E=58 keV, I_γ=19.0% γ, E=63 keV, I_γ=43.6% γ, E=110 keV, I_γ=17.4% γ, E=131 keV, I_γ=11.4 % γ, E=177 keV, I_γ=22.3 % γ, E=198 keV, I_γ=35.9 % γ, E=308keV, I_γ=10.1 %	**Direct production,** ^{168}Yb(n,γ), ^{169}Tm(p,n)	Imaging (SPECT, autoradiography) Therapeutic Dissolution studies

Activation experiment: Cu-deposited PSi

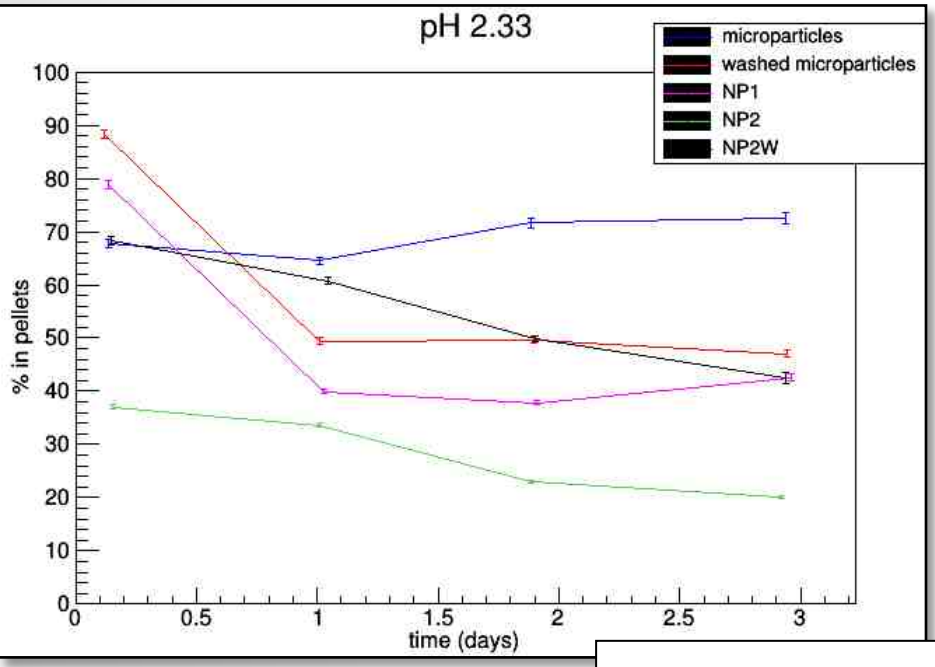
- Samples preparation at University of Turku (Finland) – nanoparticles and microparticles

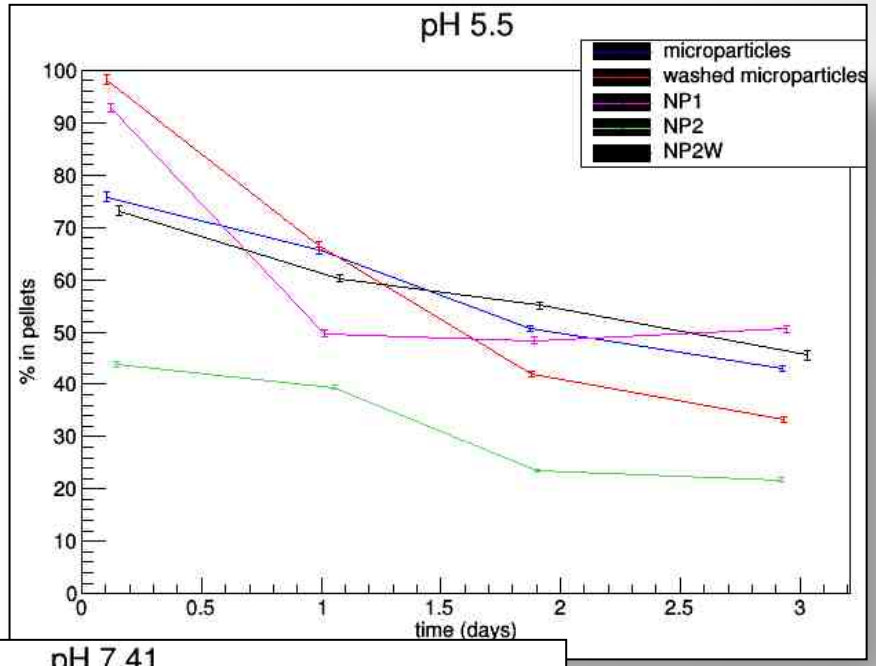
- Neutronic-activation in FiR-1 research reactor at Technical Research Centre of Finland (VTT) ($\phi_n \approx 5e12\ cm^{-2}.s^{-1}$)
  - 3h irradiation
  - Radioactive element ^{64}Cu ($T_{1/2} = 12.7$ h)

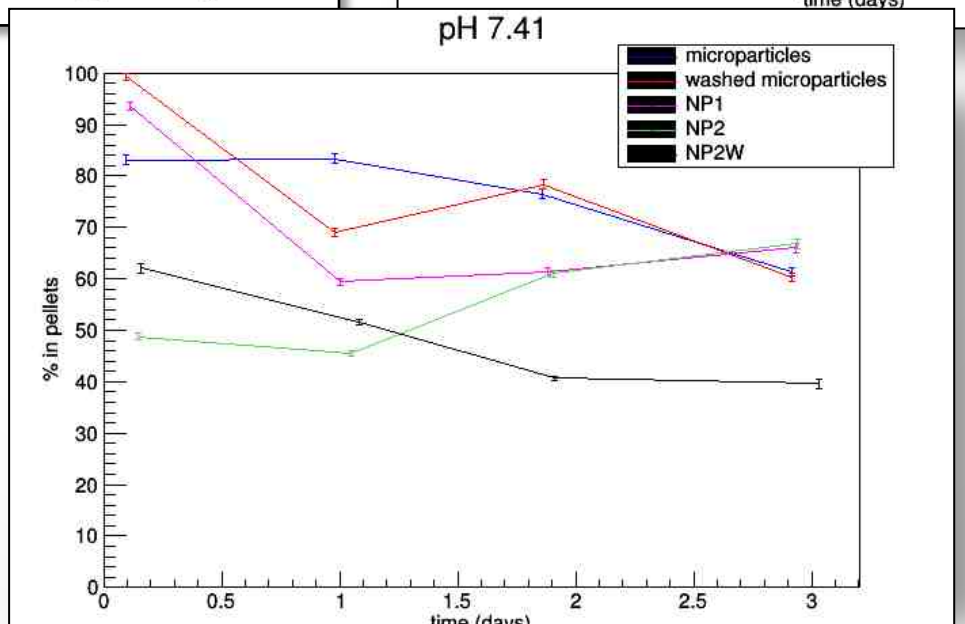
Sample	Size	Treatment	Activity (MBq)
NP1	160-170 nm	600°C annealed + native oxidation	0.920
NP2	160-170 nm	600°C annealed + thermal hydrocarbonization (THC) treatment	0,890
NP2W	160-170 nm	600°C annealed + THC treatment + HCl washing	0,440
S2	25-53 µm	600°C annealed + THC treatment	0,699
S2W	25-53 µm	600°C annealed + THC treatment + HCl washing	0,353

Dissolution/stability studies

10 mM phosphate buffers with different pH







-- microparticles
-- washed microparticles
-- NP1
-- NP2
-- washed NP2

Concentration 0.025mg/mL

Direct implantation with radioactive beam

^{169}Yb Direct implantation in PSi @ CERN

- Two silicon wafers (one fresh and one oxidized) were implanted at CERN (11/08/2015)

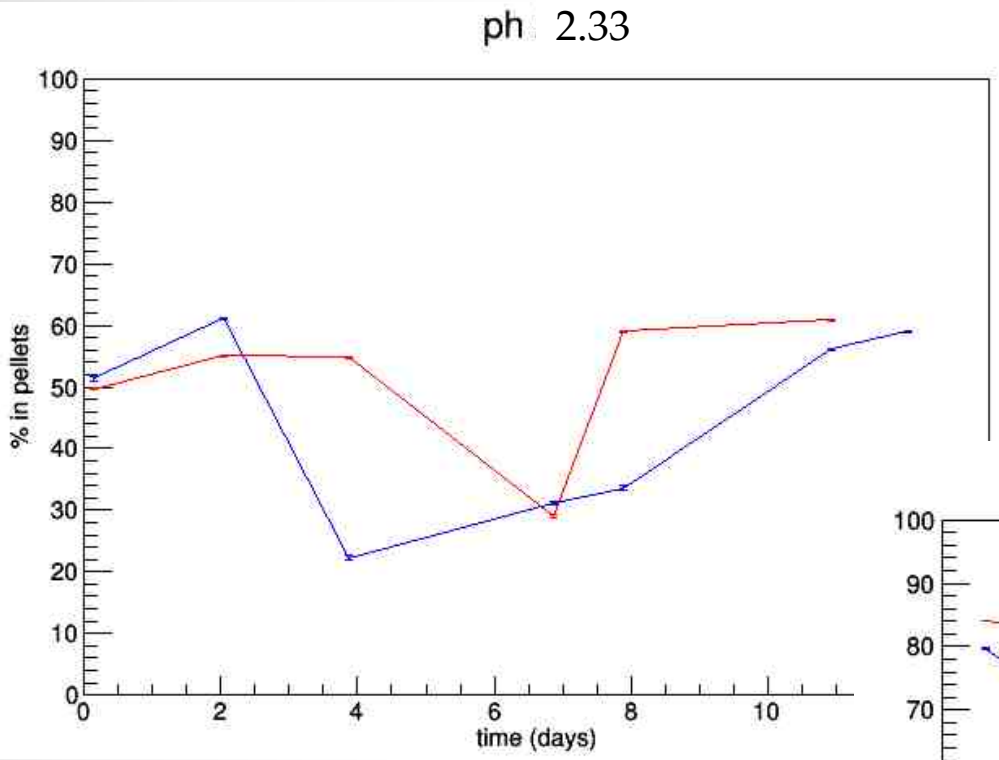
- Total activity (for the two wafers) measured by collaborators:
  - ^{169}Yb ≈ 2 MBq
  - ^{169}Lu ≈ 1 MBq
  - ^{153}Tb ≈ 6 MBq as a molecular sideband

- Total activity on 31/08/2015
  - Fresh wafer
    - ^{169}Yb = 0,6642(4) MBq
    - ^{153}Gd = 0,1452(5) MBq
    - ^{153}Tb = 0,0065(1) MBq
  - Oxidized wafer
    - ^{169}Yb = 0,5385(5) MBq
    - ^{153}Gd = 0,0816(5) MBq
    - ^{153}Tb = 0,0052(1) MBq

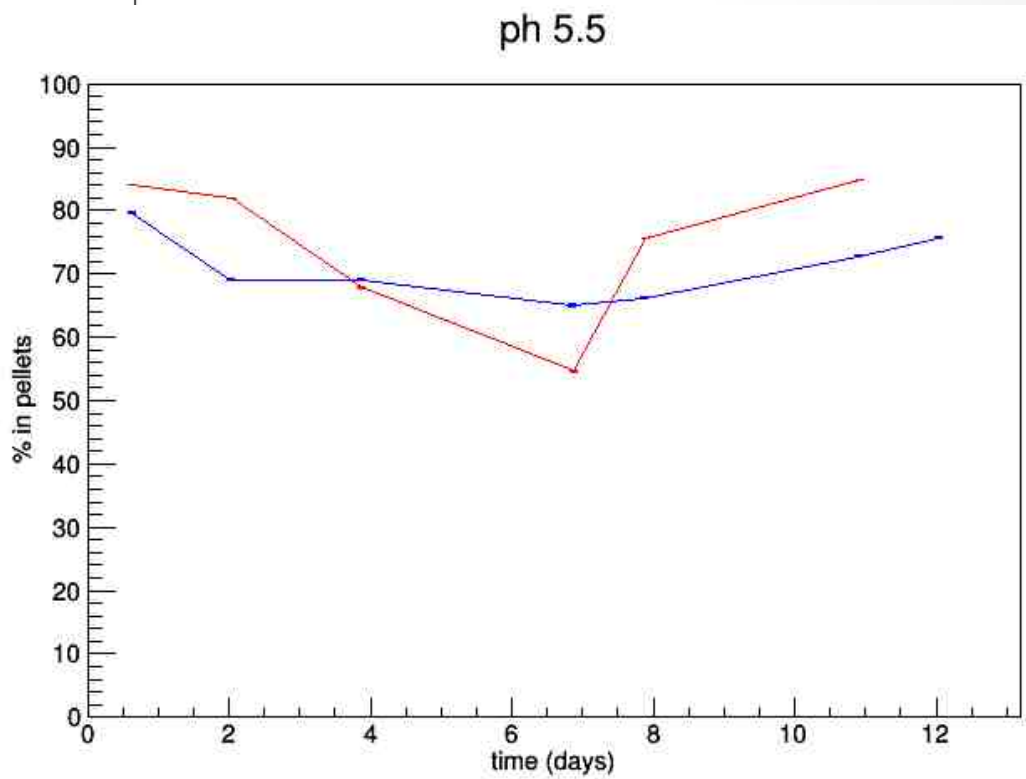
^{169}Yb

Dissolution studies: results

10 mM phosphate buffers with pH 2.33 & 5.5



Analysis on the 177 keV, 198 keV & 308 keV γ-transitions

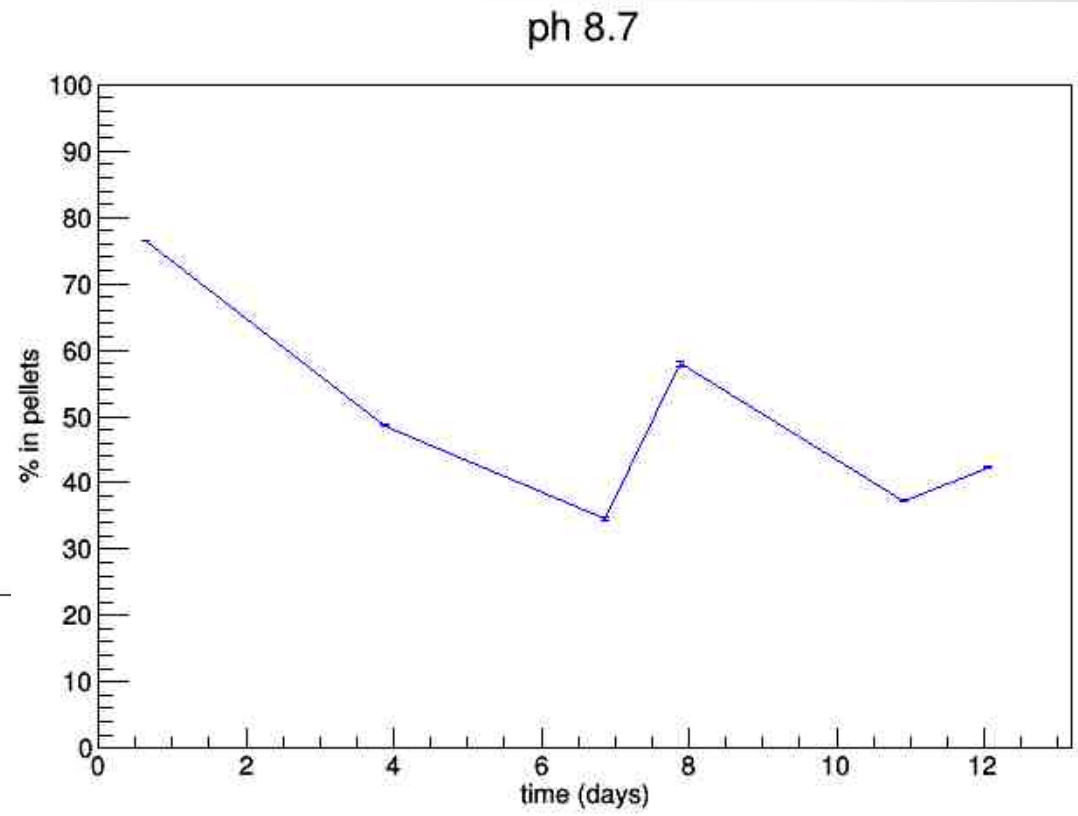


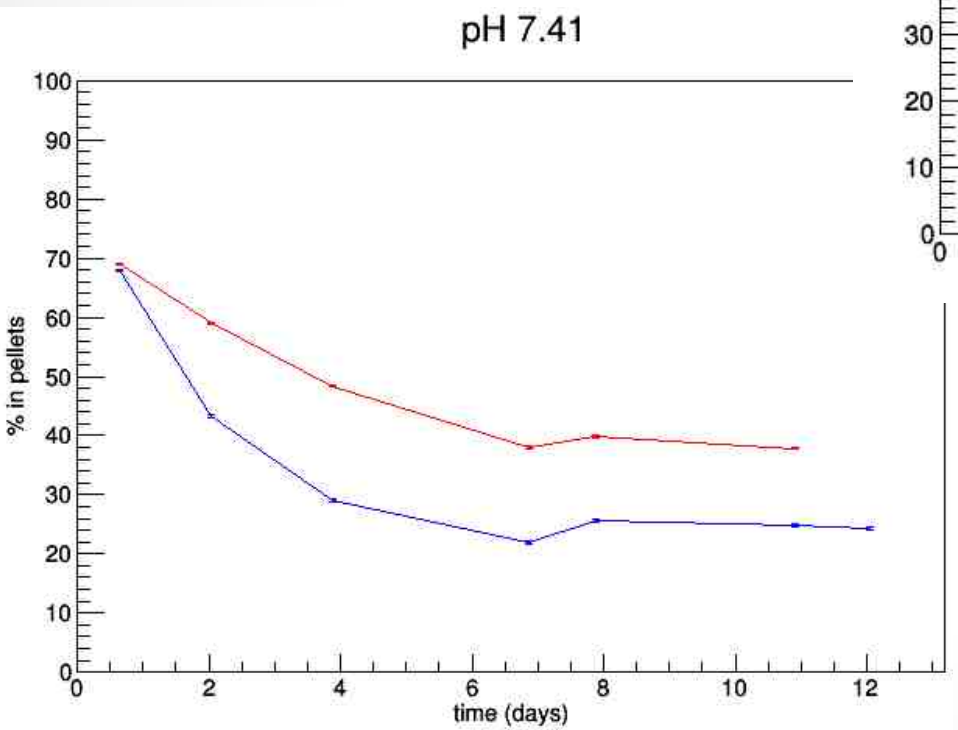
-- Fresh
-- Oxidized

Dissolution studies: results

10 mM phosphate buffers with pH = 7.41 & 8.7

-- Fresh
-- Oxidized





Conclusion & Perpectives

- Development of the experimental protocol for direct implantation
  → coating treatment after implantation will be tested
  → Longer dissolution studies to be planned

- Smaller amount of activity in washed particles - Washing effect is important during the first 24h

- Several particles candidates seems to reach a stabilized level in different pH after few days

  - in pH 5.5 and 7.41 the particles themselves dissolve whereas in pH 2.33 the Cu dissolves from the PSi

→ new stabilization treatments to improve this result.

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Thank you

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