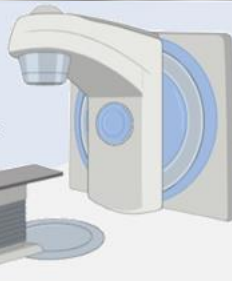


GOLD NANOPARTICLES AS THERAPEUTIC AGENT FOR RADIOTHERAPY OF PC3 PROSTATE CANCER CELL LINE

Soares, S.^{1,4}, Guerreiro, S.G.^{1,3,7,8}, Sales, M.G.F.^{1,5,11}, Correa-Duarte, M.^{1,4,13}, Fernandes, R.^{1,14}

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INTRODUCTION

- Radiotherapy (RT) is one of the most used approaches in patient's treatment with prostate cancer (PCa).¹
- Besides the evolution of equipment and technology, this therapy still has some limitations and nanotechnology can help to overcome these problems.²
- Over the years, gold nanoparticles (AuNP) have attracted a lot of interest in cancer therapies due their unique properties (Figure 1).^{3,4}

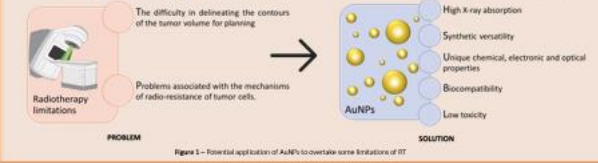


Figure 1 – Potential application of AuNP to overcome some limitations of RT

MAIN GOAL

The principal goal of this work was compared two different types of AuNPs – spherical (AuNP_s) and rods (AuNP_r) as potential radiosensitizing agents in human prostate cancer cell line (PC3) in radiotherapy treatment.

MATERIALS AND METHODS

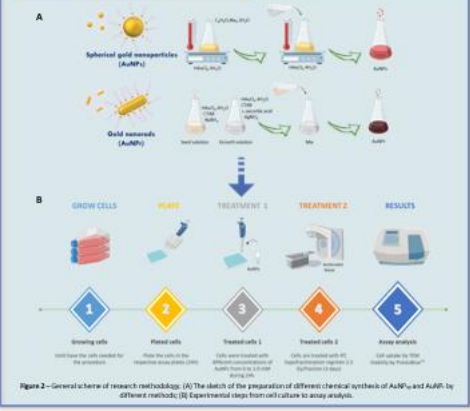


Figure 2 – General scheme of research methodology: (A) The sketch of the preparation of different chemical synthesis of AuNP_s and AuNP_r by different methods; (B) Experimental steps from cell culture to assay analysis.

CONCLUSION

- Our results showed that the shape of AuNPs influence the response to RT.
- This is the first study evaluated the effect of shapes of AuNPs as potential radiosensitizing agent in PC3 cells (prostate cancer cells).
- AuNP_r and AuNP_s demonstrated to be effective to reduce the cell viability when associated to RT.
- Comparing both nanostructures, AuNP_r demonstrated better results and a higher dose-dependency with and without radiation.

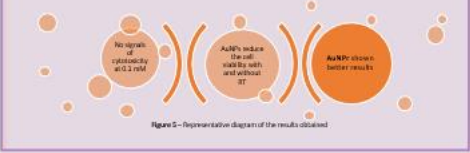


Figure 3 – Representative diagram of the results obtained

ACKNOWLEDGMENTS

Bilva Soares is grateful for the financial support of Fundação para a Ciência e Tecnologia (grant reference: SFRH/BQ/136271/2018) and thanks the kind collaboration of all those involved in the radiotherapy service at Centro Hospitalar Universitário de São João for carrying out radiotherapy treatments.

RESULTS

AuNPs characterization

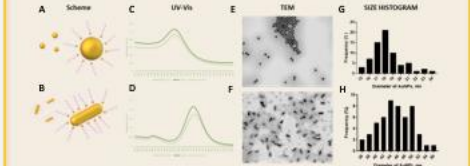


Figure 3 – Scheme of AuNP with PEG (A, B), UV-Vis spectra with and without PEG (C, D), and Transmission electron microscopy images – TEM (E, F) images of AuNP with PEG staining with phosphotungstic acid (PTA) and size histogram based TEM images (G, H). The size histograms were obtained by counting over 50 particles.

AuNPs uptake in PC3 cell lines

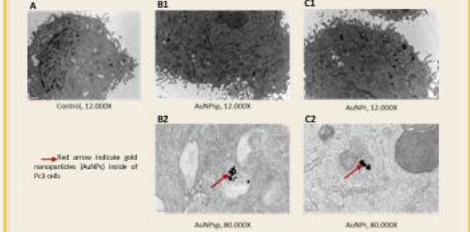


Figure 4 – TEM images of cellular uptake of AuNPs of different shapes in PC3 cells incubated with 20 μM Au³⁺ concentration. (A) represents PC3 cells without treatment; (B) and (C) represent the normal morphological appearance of PC3 cells when treated with AuNP_s and AuNP_r, respectively; (B1 and B2) and (C1 and C2) represent AuNPs taken up by PC3 cells, treated with AuNP_s and AuNP_r, respectively. Scale bar: (A, B1, C1) 5 μm and (B2, C2) 200 nm.

Effect of AuNPs in radiosensitivity of PC3 cells

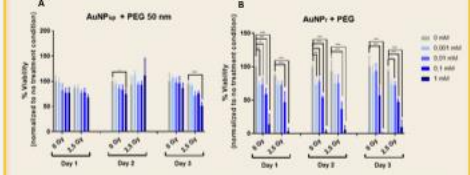


Figure 5 – Effect of AuNPs and ionizing radiation (R) on the viability of PC3 cell line – (A) and (B) represent the viability related with AuNP_s and AuNP_r respectively. The cells were treated with different concentrations (0–20 nM) for 240 prior to being exposed to a cumulative dose of 2.5 Gy in three fractions of 2.5 Gy with 600y photon beam. Cell viability (%) was measured 24h post-irradiation using the PrestoBlue assay. Results are expressed as the mean ± SD of 3 replicates. Significance of different treatments compared to control of the respective day is represented by black lines shown as *p < 0.05, **p < 0.01, ***p < 0.001 and ****p < 0.0001.

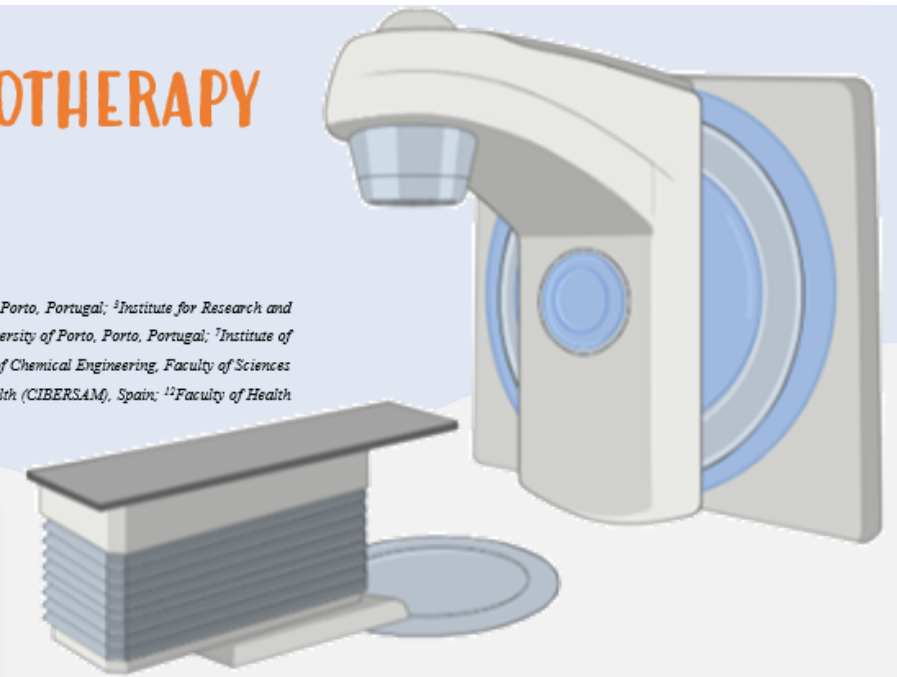


¹Morre F, Singh RSN, Brown E, Bourke L, Corbett P, Sirohi A, et al. CAU-13170-ESUR-000 Guidelines on Prostate Cancer, 2018. ²Iskovic H, Singh H, Moroni S, Trajuga E, Horiguchi K, Horiuchi Y. Understanding the mechanistic underlying the acquisition of radioresistance in human prostate cancer cells. Oncology Letters 7 (3), 2015. ³Cheng Y, Zhang S, Wang Y, Song H, Wang X, Wang Y, et al. Gold Nanoparticles in Drug-Delivery and Therapeutics for Human Cancer. Int J Mol Sci 2016;17(7):1170. ⁴Harashina M, Harashina H, Harashina H, Harashina H, Harashina H, Harashina H, et al. Synthesis of gold nanoparticles and their application in gene functionalization. Journal of Nanoparticles 2015;2015:1-2.

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¹BioMark-CEB/ISEP, Polytechnic of Porto, Porto, Portugal; ²LaBMI – Laboratory of Medical & Industrial Biotechnology, Porto Research, Technology & Innovation Center (PORTIC), P.PORTO – Polytechnic Institute of Porto, Porto, Portugal; ³Institute for Research and Innovation in Health (i3S), Porto, Portugal; ⁴Faculty of Chemistry, University of Vigo, Vigo, Spain; ⁵CEB, Centre of Biological Engineering of Minho University, Braga, Portugal; ⁶School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal; ⁷Institute of Molecular Pathology and Immunology of the University of Porto-IPATIMUP, Porto, Portugal; ⁸Department of Biomedicine, Biochemistry Unit, Faculty of Medicine, University of Porto, Porto, Portugal; ⁹Biomark/UC, Department of Chemical Engineering, Faculty of Sciences and Technology, University of Coimbra, Coimbra, Portugal; ¹⁰CINBIO, University of Vigo, 36310 Vigo, Spain; ¹¹Southern Galicia Institute of Health Research (IISGS), and Biomedical Research Networking Center for Mental Health (CIBERSAM), Spain; ¹²Faculty of Health Sciences (FCS) & Hospital Escola Fernando Pessoa (HEFP), University Fernando Pessoa (UFP), Porto, Portugal



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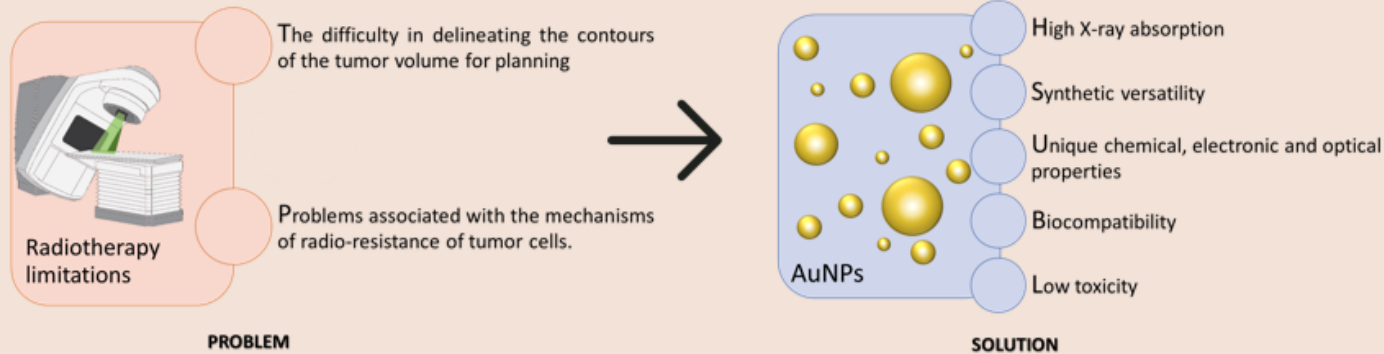


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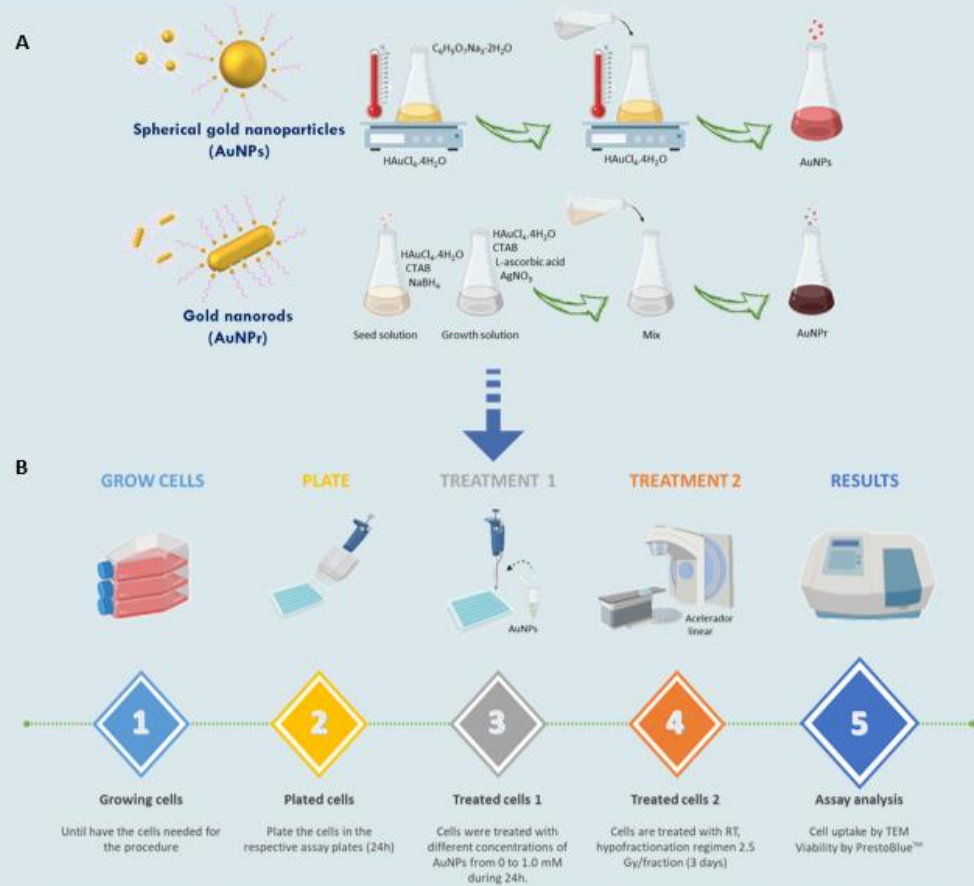


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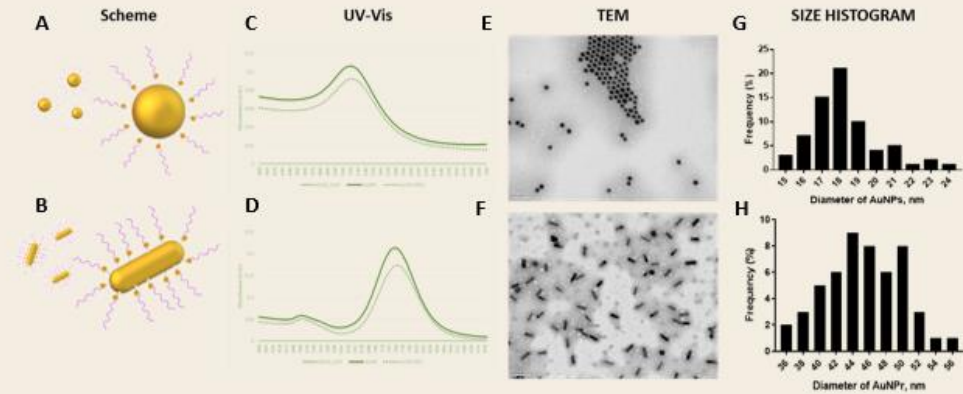


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AuNPs uptake in PC3 cell lines

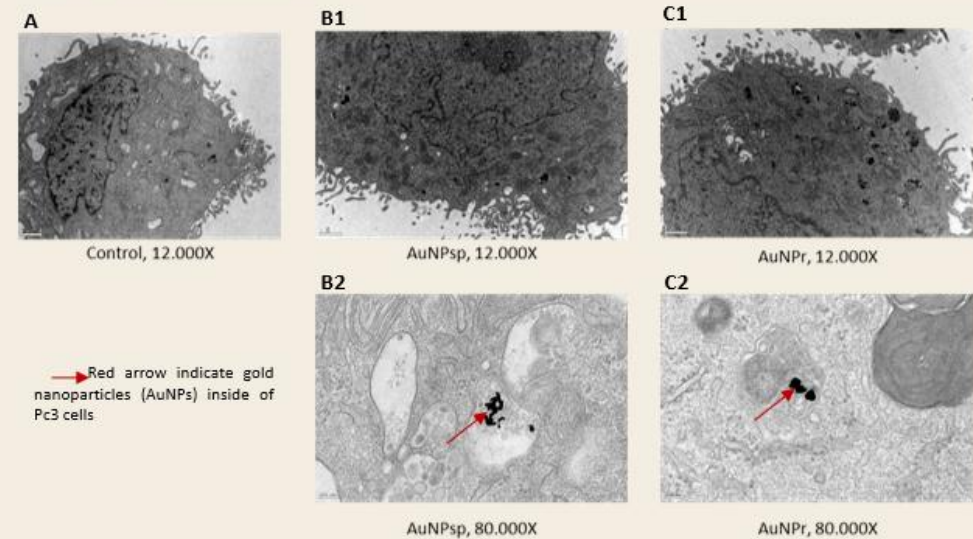


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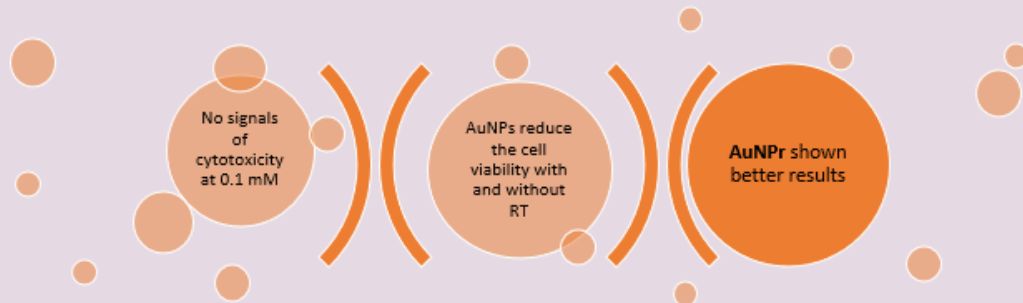


Figure 5 – Representative diagram of the results obtained

Effect of AuNPs in radiosensitivity of PC3 cells

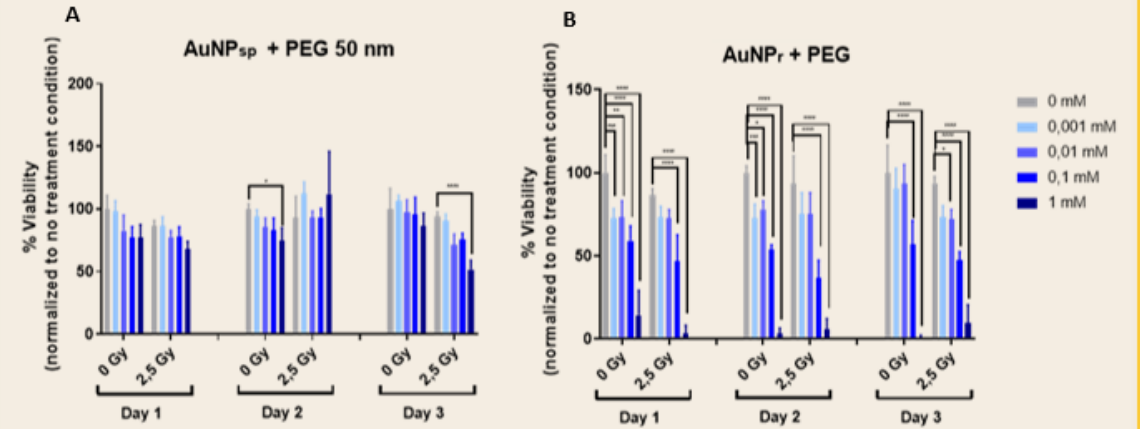


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- ¹ Mottet N, Bergh RCN, Briers E, Bourke L, Cornford P, Santis M, et al. EAU-ESTRO-ESUR-SIOG Guidelines On Prostate Cancer, 2018; ² Murata, K., Saga, R., Monzen, S., Tsuruga, E., Hasegawa, K., Hosokawa, Y. "Understanding the mechanism underlying the acquisition of radioresistance in human prostate cancer cells". Oncology Letters 17,8 2019; ⁴ Singh P, Pandit S, Mokkalapati V, Garg A, Ravikumar V, Mijakovic I. Gold Nanoparticles in Diagnostics and Therapeutics for Human Cancer. Int J Mol Sci. 2018;19(7); ⁵ Kawamura G, Nogami M, Matsuda A. Shape-controlled metal nanoparticles and their assemblies with optical functionalities. Journal of Nanomaterials. 2013;2013:2.