

Gold nanoparticles: a promising next-generation tool for breast cancer photothermal therapy

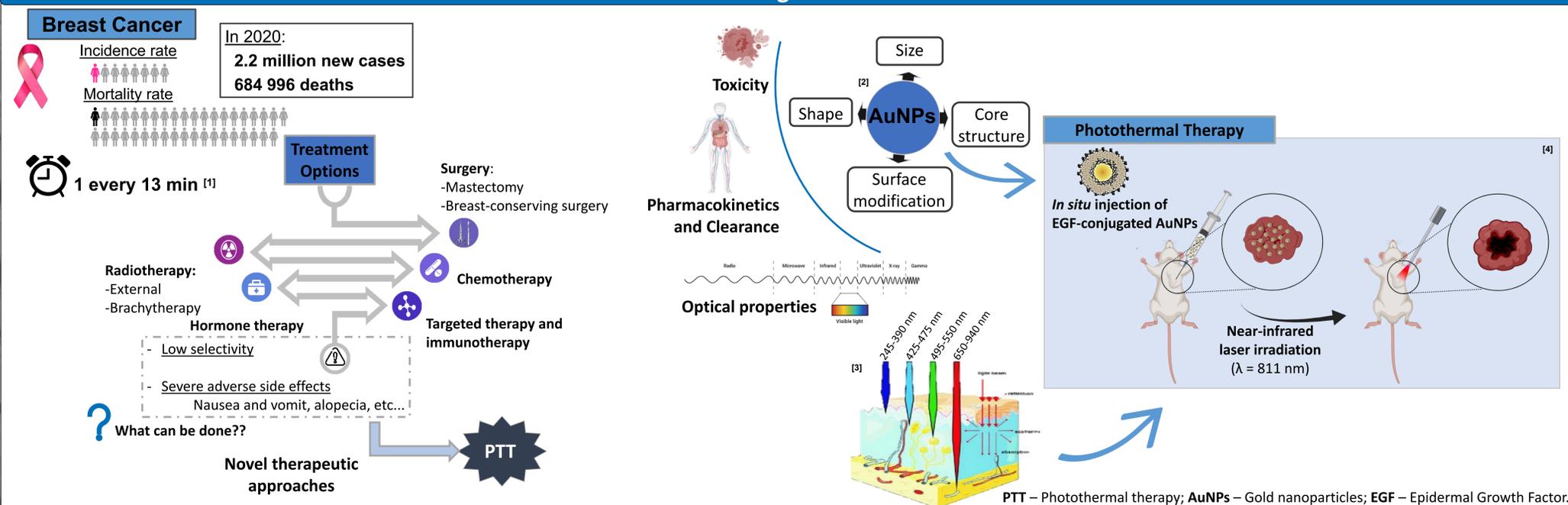
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Background



Results

AuNPs Synthesis and Characterization

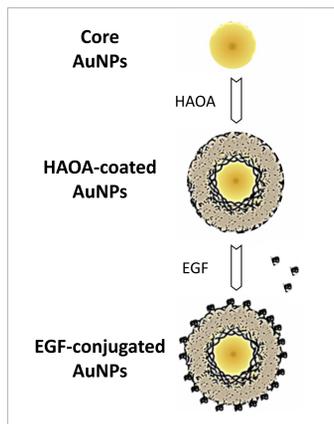


Table 1. AuNPs characterization. Size and Pdl determined by DLS and Maximum Absorbance Peak by UV-Vis spectroscopy.

AuNPs	Main Peak (nm)	Pdl	Maximum Absorbance Peak (nm)
Core	252.4 ± 9.3	0.73 ± 0.02	899 ± 1
HAOA-coated	334.4 ± 40.4*	0.64 ± 0.09	A broad band
EGF-conjugated	191.6 ± 17.3##	0.38 ± 0.02***,##	823 ± 1

Size and Pdl represented as Mean ± SD (n = 3), and maximum absorbance peak as the single value detected by the equipment ± the equipment uncertainty. Statistical analysis: * p<0.05; *** p<0.001 comparing with the Core AuNPs and ## p<0.01 comparing with the HAOA-coated AuNPs.

Table 2. Hemolysis (%) of Core AuNPs and EGF-conjugated AuNPs (Mean ± SD, n = 3).

AuNPs Concentration (mg/mL)	0.3 x 10 ⁻³ up to 3.5 x 10 ⁻¹	0.7
Core AuNPs	No hemolytic activity	
EGF-conjugated AuNPs	No hemolytic activity	2.0 ± 0.2

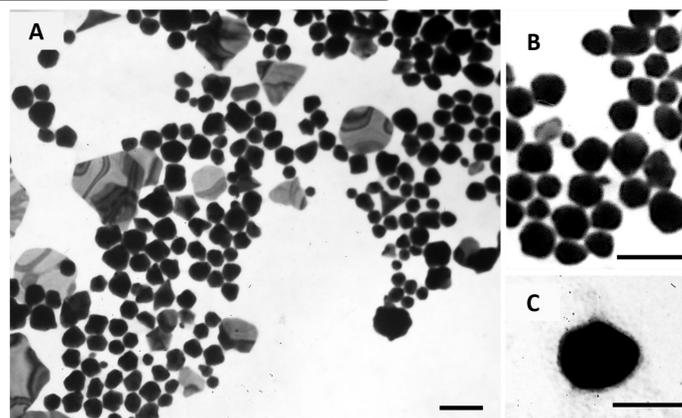


Figure 1. Morphological characterization of Core AuNPs (A and B) and EGF-conjugated AuNPs (C) by TEM. (B) shows with more detail the spherical-like shape of Core AuNPs. Scale bars = 100 nm.

PTT efficacy

In vitro

Cell Line	Main Characteristics
MCF-7	Human adenocarcinoma of the breast, ER+, PR+ and HER2-
MDA-MB-231	Human adenocarcinoma of the breast, ER-, PR- and HER2-
Triple-negative	Less treatments available Harder to treat

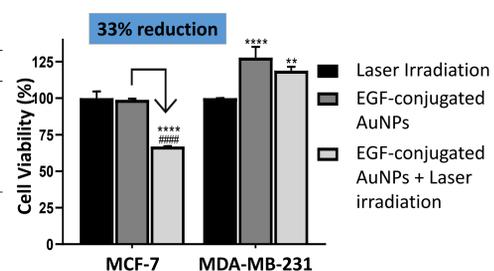


Figure 2. Cell viability (%) of MCF-7 and MDA-MB-231 cells treated with laser irradiation (5.6 ± 0.2 W/cm², 3 min) and/or EGF-conjugated AuNPs (incubated with 50 μM of gold for 4 h). Results represented as Mean ± SD (n = 3). Statistical analysis: ** p < 0.01; **** p < 0.0001 comparing with the cells subjected to the laser irradiation and #### p < 0.0001 comparing with the cells incubated with EGF-conjugated AuNPs alone.

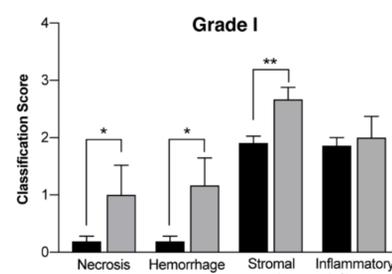
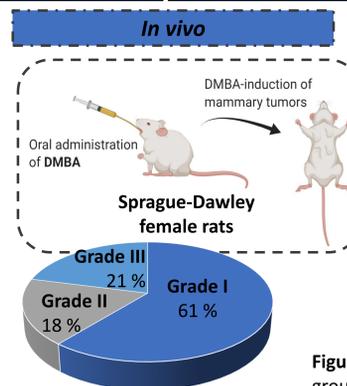


Figure 4. Histological evaluation of Grade I mammary tumors in a group without treatment (black columns) and in a group treated with EGF-conjugated AuNPs and laser irradiation (grey columns). Results represented as Mean ± SEM and statistically significant differences are identified with * p < 0.05 and ** p < 0.01.

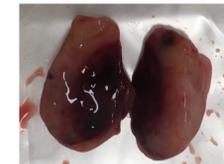


Figure 3. Photography of a representative excised tumor with visible hemorrhagic area after treatment with EGF-conjugated AuNPs and laser irradiation (tumor grade I, scale bar 0.5 cm).

No morphological changes in non-target-organs!

Conclusions

- ✓ AuNPs show suitable mean sizes and maximum absorbance peaks to be used for PTT when locally administered.
- ✓ AuNPs show no toxicity either in breast cancer cell lines or red blood cells.
- ✓ Laser irradiation proved to be safe when applied alone.
- ✓ Combining EGF-conjugated AuNPs with laser irradiation resulted in a reduction of 33% in MCF-7 cells viability.
- ✓ The animal model was successfully developed (all animals developed tumors) and proved to be a specific model for breast cancer, once no other alterations were observed in other organs.
- ✓ *In situ* administration of EGF-conjugated AuNPs combined with laser irradiation resulted in tumor necrosis with minimal or absent effects over surrounding healthy cells.
- ✓ This system revealed great potential to expand breast cancer treatment options. Nevertheless, further research is required to assess if this strategy can be applied as an adjuvant technique to surgical intervention, improving, at least, esthetic outcomes, or applied alone when other therapies are not viable, safe, or acceptable.

Acknowledgements

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References

- [1] American Cancer Society. Breast Cancer Facts & Figures. Available online: <https://www.stopbreastcancer.org/information-center/facts-figures/> (accessed on 30 January 2023).
- [2] Ferreira-Gonçalves, T., Ferreira, D., Ferreira, H.A., Reis, C.P., Nanomedicine. 2021, 16, 2695-2723.
- [3] Agostinis, P., Berg, K., Cengel, K.A., Foster, T.H., Girotti, A.W., Gollnick, S.O., Hahn, S.M., Hamblin, M.R., Juzeniene, A., Kessel, D., et al., CA: A Cancer Journal for Clinicians, 2011, 61, 250-281.
- [4] Costa, E., Ferreira-Gonçalves, T., Cardoso, M., Coelho, J.M.P., Gaspar, M.M., Faisca, P., Ascensão, L., Cabrita, A.S., Reis, C.P., Figueiredo, I. V., Int. J. Mol. Sci.. 2020, 21(24), 9681.