Evaluating Gold Nanoparticles for Preoperative SABR Treatment Planning of Intact Breast Cancer: From Imaging and Planning to Radiosensitization

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ABSTRACT

Purpose: To evaluate the feasibility of using a 4.2 MV imaging beam for simultaneous guidance and biologically enhanced delivery of preoperative stereotactic ablative radiotherapy (SABR) to intact breast tumors loaded with gold nanoparticles (AuNPs) and evaluate the expected radiosensitization effect.

Methods: We assessed physical contrast and biological radiosensitization for a 4.2 MV-CBCT beam (Siemens ONCOR) against a standard 6 MV flattening-filter-free (FFF) beam. First, we imaged 15 nm AuNPs at different concentrations up to 20 mg Au/mL in a breast phantom using diagnostic CT and 4.2 MV-CBCT to determine detectability. Second, we performed EGSnrc-based Monte Carlo treatment planning for two intact breast cases (20–24 Gy single-fraction), comparing AuNP-enhanced coplanar IMRT plans, modeling both intratumoral and intravenous distributions of AuNPs, against clinical non-coplanar 4π SABR benchmarks. We quantified target coverage, homogeneity index (HI), and organ-at-risk (OAR) sparing. Finally, we measured in vitro radiosensitization by quantifying γH2AX DNA damage foci in MDA-MB-231 cells irradiated (0–3 Gy) with and without AuNPs.

Results: AuNPs produced segmentable contrast in both diagnostic CT (~600 HU above tissue background) and MV-CBCT (~50 HU), facilitating target definition even with the spectral hardening. In planning studies, AuNP-enhanced coplanar IMRT improved dose homogeneity (HI improved from 0.34 to 0.21) and decreased dose spill-off (GTVrim spill-off reduced from 35% to 3%) relative to 4π SABR benchmarks, while maintaining heart and lung doses below toxicity threshold (mean dose <1 Gy). Moreover, the 4.2 MV beam yielded a higher biological effect, with a radiosensitization factor of 1.51 ± 0.09 compared to the 6 MV-FFF beam 1.33 ± 0.07 ($p<0.001$), confirming the spectral advantage of the lower energy beam driven by photoelectric absorption.

Conclusion: Repurposing a low-energy 4.2 MV IGRT beam for AuNP-loaded breast tumors achieves superior radiosensitization and sufficient imaging contrast, enabling simplified coplanar SABR workflows without compromising plan quality.

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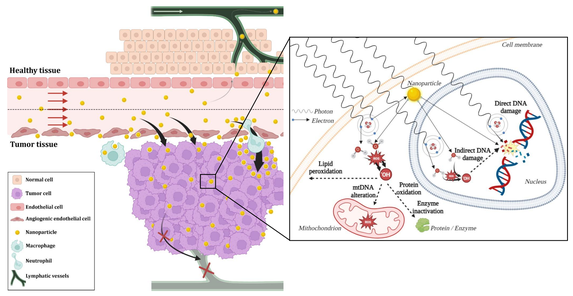
INTRODUCTION

Gold nanoparticles (AuNPs) act as **theranostic agents** in radiotherapy when located selectively in the tumor. They provide enhanced CT **contrast** of the lesion while they act as **dose enhancers** and **radiosensitizers**.



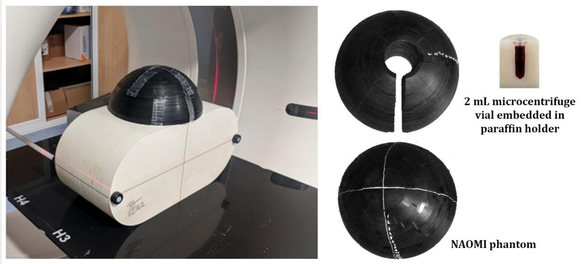
Single-session **SABR for intact breast tumors** has been reported in a few trials, with early findings showing both promises and ongoing difficulties, often requiring challenging beam geometrical arrangement and advanced delivery technology.

The breast setup is specifically favorable for AuNP-mediated dose enhancement, and AuNPs could help with plan optimization and enable simpler planning approaches.

Here, we propose using a low energy MV beam both for imaging and treatment, while we show an additional radiosensitization benefit.

METHODOLOGY

1. We **imaged** AuNPs on a breast cancer phantom at different concentrations on both a CT and a 4.2 MV-CBCT scanner.



2. We performed Monte Carlo **treatment planning** (EGSnrc) of two intact breast SABR clinical cases virtualizing AuNP in the tumors.
3. We evaluated **radiosensitization** in terms of γH2AX DNA damage foci in MDA-MB-231 cells in the presence or absence of AuNPs.

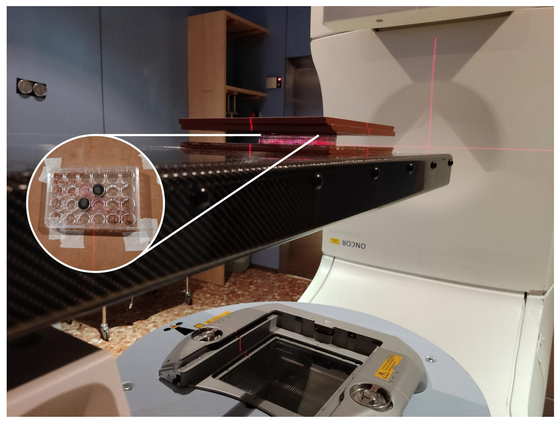
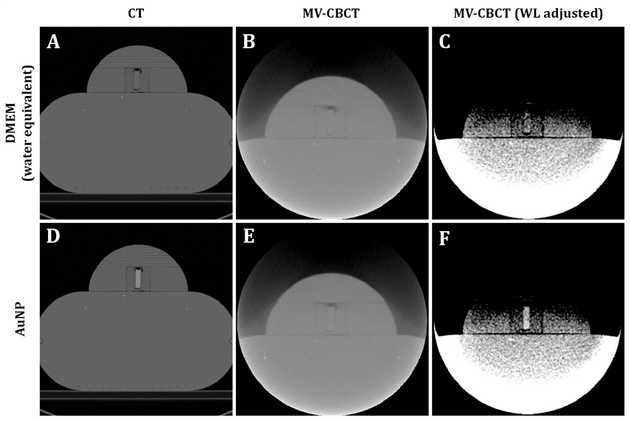


IMAGE CONTRAST

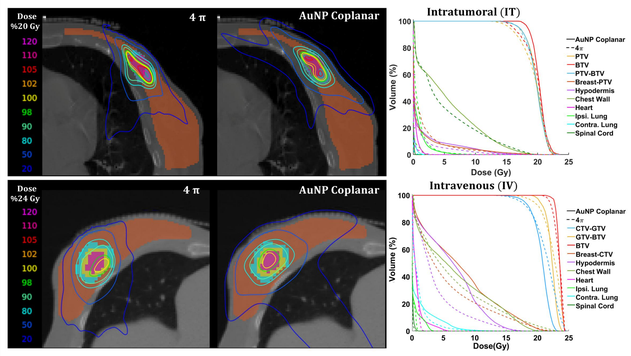
CT contrast is remarkably enhanced and visible naked-eye, even without adjusting the window level. Absolute CT-number difference is **~600 HU** over water for a concentration of 20 mg Au/cm^3 (figure panels A, D).

MV-CBCT contrast is subtle when displayed over the full dynamic range (figure panels B, E) but remains detectable at the same concentration with a CT-number difference of **~50 eqHU**, and a window level adjustment renders it discernible (figure panels C, F). Three-dimensional **automatic segmentation** of the AuNP volume shows close agreement with the real volume in the vial (99.5%).



TREATMENT PLANNING

The presence of AuNP translates into a **dose enhancement factor** (DEF) of up to **~15%.** This DEF was leveraged to optimize the dose distribution. We report theoretical distributions of AuNP for both intratumoral (IT) and intravenous (IV) delivery.



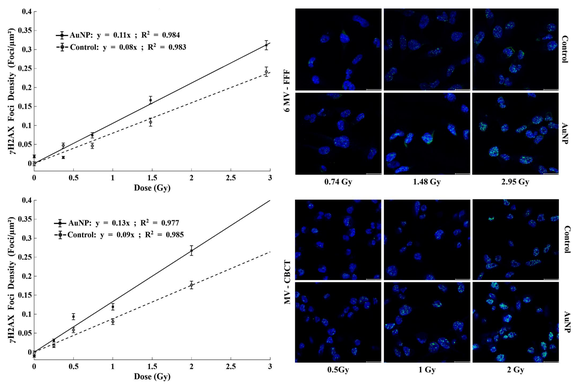
	Left Breast (IT)				Right Breast (IV)					
	BTV		PTV-BTV		BTV		GTV-BTV		CTV-GTV	
	4π	AuNP-CRT	4π	AuNP-CRT	4π	AuNP-CRT	4π	AuNP-CRT	4π	AuNP-CRT
D_{max} (Gy)	22.7	23.6	22.8	23.6	24.4	24.4	24.5	24.1	24.6	23.5
D_{mean} (Gy)	19.8	20.3	19.5	19.8	23.0	23.5	22.5	22.3	21.4	20.6
D_{95} (Gy)	16.2	18.4	15.2	16.5	22.0	22.7	19.5	20.4	17.5	18.0
$100(D_{95}-D_p)/D_p$(%)	-19	-8	-24	-18	-8	-5	-19	-15	-27	-25
Spill-off* 95 (%)	68	62	55	51	68	33	35	3	2	0
Spill-off* 90 (%)	73	69	60	56	78	66	47	23	7	3
HI	0.34	0.23	0.41	0.32	0.12	0.08	0.23	0.16	0.29	0.26

*Spill-off values were computed over the entire target volumes: PTV, CTV and GTV

Overall, **AuNP** were able to **simplify the treatment** to conventional coplanar RT, while **increasing** the **target coverage**, **decreasing** the dose **spill-off**, and **improving** the **homogeneity index**. All the organs at risk were maintained under constraints. Thus, NTCP models did not increase the predicted risks and TCP improved, up to +51 percentage points at 10^8 cells/cm^3.

RADIOSENSITIZATION

The **radiosensitization factor** (RSF) for both MV-CBCT and 6 MV-FFF was determined as the ratio of slopes of the γH2AX foci dose-response curve with/without AuNPs.



AuNPs **radiosensitization** effect is present for both beams. **6 MV-FFF** shows an RSF of **1.33** ± 0.14 (95% CI), and the **MV-CBCT** beam shows a higher RSF of **1.51** ± 0.17 (95% CI).

CONCLUSIONS

- **A single low-energy beam can serve both for imaging and therapy**, enabling a theranostic AuNP-based SABR workflow with a single hardware platform.
- **AuNP-driven dose enhancement** (up to ~15%) **enables planning simplification** from non-coplanar 4π to coplanar IMRT, with improved homogeneity, reduced spill-off, and preserved OAR sparing.
- **Radiosensitization amplifies the physical gain** by roughly three-fold above baseline enhancement, exceeding what macroscopic DEF predicts.
- **Radiosensitization persists at 6 MV-FFF**, where no significant dose enhancement is expected. While planning optimization currently requires a beam with actionable DEF, this decoupling of radiobiological benefit points to a practical translational path on standard linacs.

LET'S CONNECT!

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