Schilling D, and her co-workers submitted their research data in this manuscript entitled “Induction of plasminogen activator inhibitor type-1 (PAI-1) by hypoxia and irradiation in human head and neck carcinoma cell lines”

It is evident from previous studies that squamous cell carcinoma of the head and neck (SCCHN) often contain highly radioresistant hypoxic regions and that approaches involving radiotherapy are common for the treatment of these tumours. Reoxygenation during fractionated radiotherapy is desired to make these hypoxic tumour regions more radiosensitive.

The authors showed successfully the kinetics of PAI-1 expression and secretion after hypoxia and reoxygenation, and determined the influence of ionizing radiation on PAI-1 levels in vitro, in the two human squamous cell carcinoma of the head and neck cell lines (SCCHN), squamous cell carcinoma cell line (BHY) and human squamous carcinoma cell line (FaDu), and it is first time to show that in vitro hypoxia significantly up-regulates cellular and secreted PAI-1 protein levels after short exposure times and continues up to 24 h in two SCCHN cell lines with an analogous PAI-1 up-regulation by hypoxia in both cell lines, BHY and FaDu.

The data suggest that both, short term and long term hypoxic exposure could increase PAI-1 levels in SCCHN. We have here to mention that the results obtained by this research group show also ionizing radiation induces PAI-1 expression and secretion in SCCHN cell lines. This leads to a further knowledge point that radiation therapy that represents a common treatment approach for hypoxic head and neck tumours lead to enhanced PAI-1 expression and secretion in vivo. Further, since PAI-1 is involved in tumour invasion and migration, therefore, fractionated radiotherapy could lead to a more aggressiveness of tumour cells, which are not killed immediately with subsequent lead increased metastasis.

Data suggest that in vivo already that acute hypoxia might be sufficient to up-regulate PAI-1 in SCCHN. Regarding radioresistance, acutely hypoxic cells are believed to be a more serious problem than chronically hypoxic cells. Acute hypoxia might be harmful in two ways; on the one hand by causing radioresistance and on the other hand by increasing PAI-1 levels, which most likely leads to a more aggressive phenotype of the surviving radioresistant cells.

Results confirm previous in vitro studies showing enhanced PAI-1 transcription and expression after ionizing radiation in non-transformed rat tubule epithelial cells and increased PAI-1 transcription in human hepatoma cells in vitro and in vivo studies have also demonstrated HIF-1??induction by radiation. They also speculate that radiation induced PAI-1 upregulation might occur via HIF-1?.

Radiation therapy, which is a common treatment modality for the frequently hypoxic head and neck tumours, could lead to enhanced PAI-1 expression and secretion in vivo since, results show, that not only hypoxia but also ionizing radiation induces PAI-1 expression and secretion in SCCHN cell lines. This study represent a contribution to the basic and clinical informations related to hypoxia regulated cancer and radiation therapy in cancer. They also showed, that reoxygenation of hypoxic tumour cells during fractionated radiotherapy could be favourable by counteracting the increased PAI-1 levels.

In my opinion, the knowledge obtained from the data presented in this manuscript represent an original contribution to the research in this field. Therefore, I recommend publishing this manuscript submitted by Schilling D and her collaborators, in BMC Cancer.

Also I would like to wish this study group a lot of success in their future studies.

What next?: Accept without revision
Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I also declare that competing interests does not exist.