Viral gene therapy could improve results from breast reconstruction after cancer treatment

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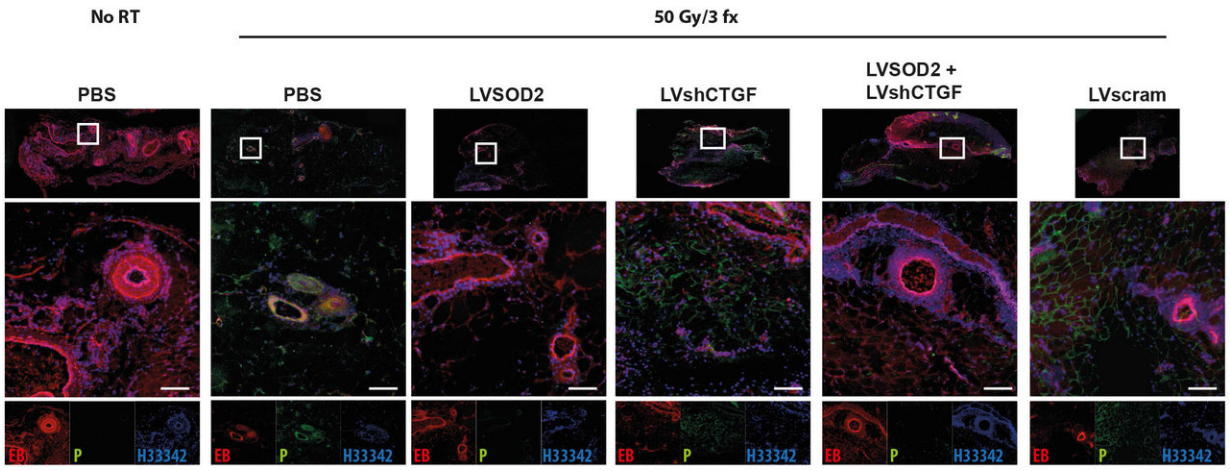


Scientists used gene therapy to protect blood vessels from radiation damage, which could improve outcomes for reconstructive surgeries for breast cancer. Credit: A.A. Khan et al., *Science Translational Medicine* (2018)

A new type of gene therapy delivered using a virus could protect healthy tissues from the harmful side-effects of radiotherapy after cancer treatment, a new study reports.

In the future, the treatment could be used to improve outcomes for breast reconstruction surgery in women with breast cancer - by

protecting patients from scarring, shrinkage of the skin and damage to the underlying tissues.

Scientists at The Institute of Cancer Research, London, found they could prevent tissue damage in rats treated with radiotherapy by reprogramming healthy cells to protect themselves.

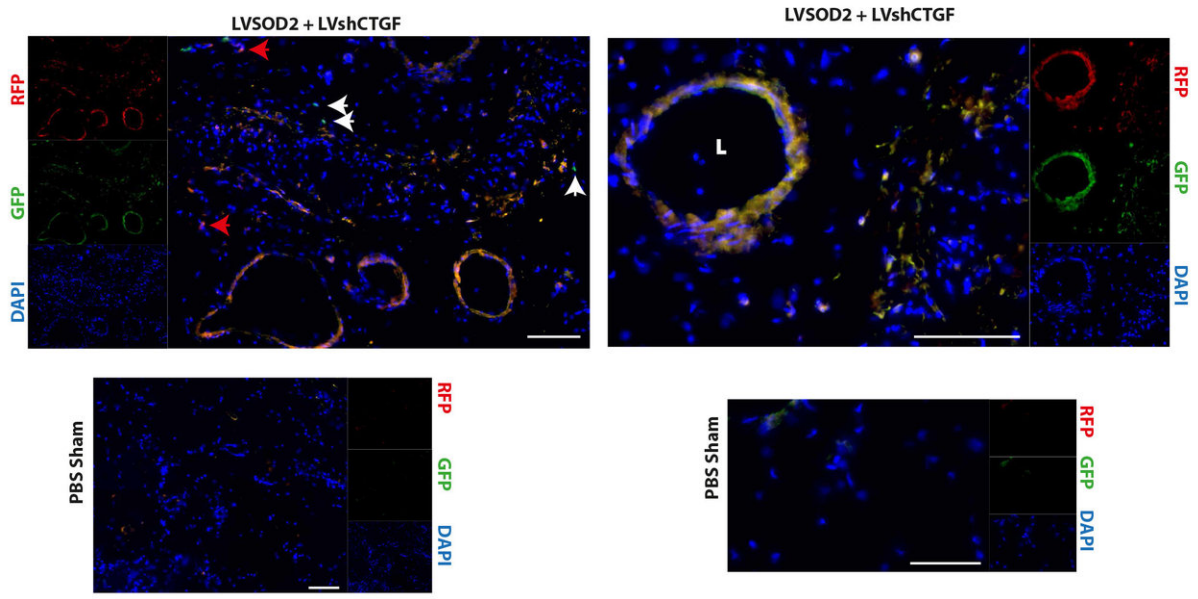
Modern radiotherapy is increasingly precise and targeted, but even so it can still cause a variety of side-effects to tissues including skin, fat and blood vessels, months or years after treatment.

The protection given by the new gene therapy could prevent radiotherapy side-effects in women who have had breast reconstruction surgery, and spare women a second operation to repair the damage caused by delayed side-effects.

The study is published today (Wednesday) in the journal *Science Translational Medicine*, and was largely funded by the Wellcome Trust.

The team at The Institute of Cancer Research (ICR), in collaboration with plastic surgeons at The Royal Marsden NHS Foundation Trust, injected rats with a modified and harmless version of a type of virus called a lentivirus.

The virus was used to deliver extra copies of a gene called SOD2, which plays a role in limiting the stress response to the harmful particles released by radiotherapy.



Scientists used gene therapy to protect blood vessels from radiation damage, which could improve outcomes for reconstructive surgeries for breast cancer. Credit: A.A. Khan et al., *Science Translational Medicine* (2018)

The team combined this with a second virally delivered treatment to block activity of a different gene involved in the scarring response to radiotherapy, called CTGF.

Six months after radiotherapy, transplanted tissues in rats that had been treated with a combination of SOD2 and CTGF gene therapy had shrunk by just 15 per cent, compared with 70 per cent in those that had not received either treatment.

The viral therapy was injected into blood vessels in tissue before it was transplanted to ensure that the protective effect was isolated only to healthy tissue away from the cancer - and to model the situation in which the gene therapy would be delivered in the clinic.

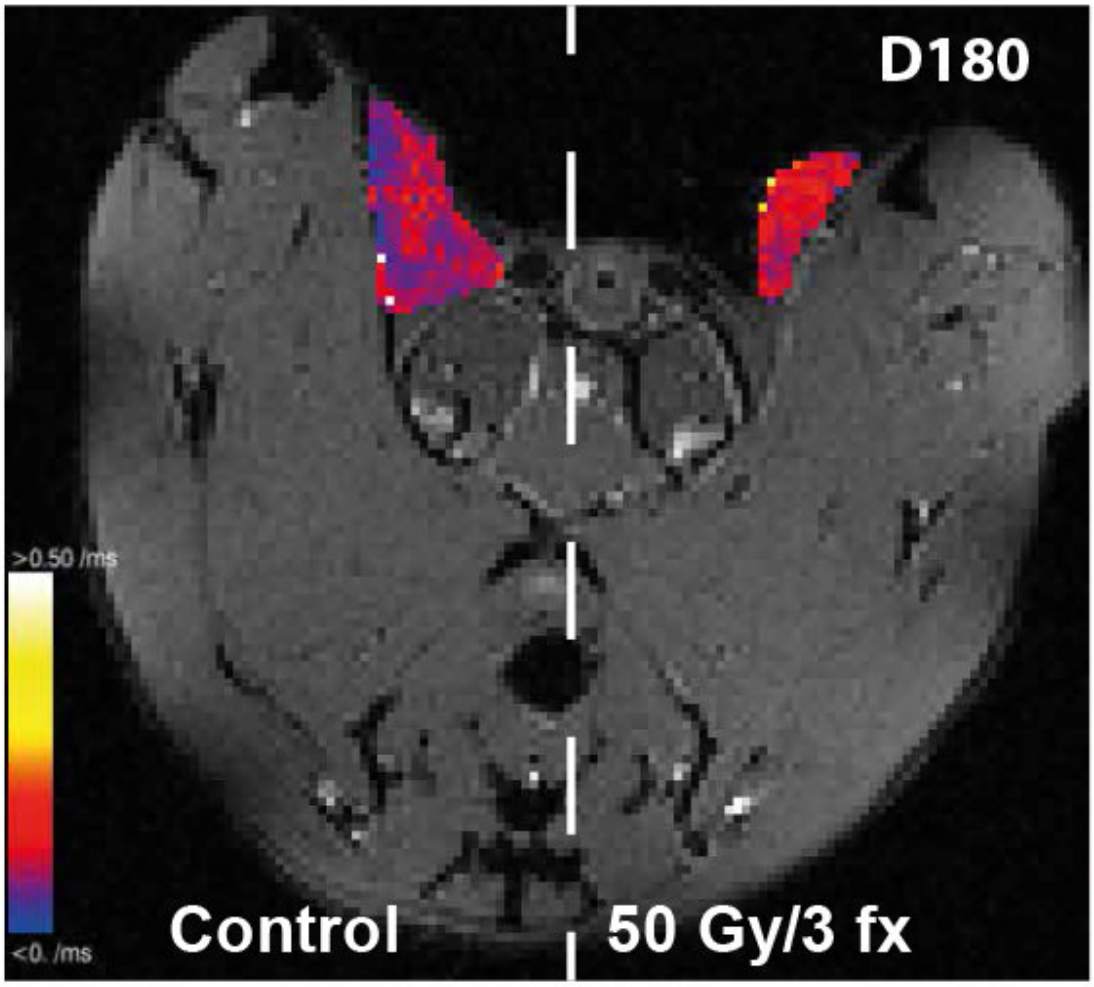
The amount of SOD2 and CTGF did not increase in the area outside the transplanted tissue - meaning that tumour cells were not protected by the treatment, and stayed vulnerable to radiotherapy.

Tumours in rats that had been treated with the gene therapy responded better to radiotherapy - with tumour growth stopped for 40 days in four out of five animals.

The findings suggest that by protecting the healthy tissues around tumours, the gene therapy increased the effectiveness of radiotherapy - although more research is needed to find out how and why this happens.

The two gene therapies targeting the CTGF gene and the SOD2 gene, respectively, seemed to counteract radiotherapy damage in healthy tissue through different mechanisms - suggesting that a combination of the two therapies would be most beneficial.

The new study opens up the possibility of offering women with breast cancer earlier reconstruction surgery, using tissues that are protected from radiotherapy side-effects. The next step will be to test out the new treatment in clinical trials.



MRI showing how radiation therapy for breast cancer can damage blood vessels. Credit: A.A. Khan et al., *Science Translational Medicine* (2018)

Professor Kevin Harrington, Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, said:

"We have developed a new viral gene therapy that can help healthy tissue protect itself from the damage caused even by modern, more precise forms of radiotherapy.

"Now that people with cancer are surviving longer, it is increasingly important to address the long-term impact of cancer treatments.

"Some women who need radiotherapy after a mastectomy have to wait up to six months after the end of their treatment before they can have breast reconstruction surgery, to allow time for side-effects to show themselves.

"In the future, we hope this new viral gene therapy could protect healthy tissue transplanted during cancer surgery, bringing forward the subsequent operation to reconstruct the breast."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"This study has found a clever new way to deliver gene therapy using a virus, so that healthy tissue is protected from radiotherapy side-effects while tumour cells remain vulnerable to the treatment.

"It's exciting that the new viral treatment has successfully protected healthy tissue and at the same time also improved outcomes in rats, and it raises the real possibility that this could become a new way of improving quality of life in cancer patients."

More information: A.A. Khan el al., "Genetically modified lentiviruses that preserve microvascular function protect against late radiation damage in normal tissues," *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aar2041

Provided by Institute of Cancer Research