



RESEARCH

INFORMATION

## Microwave treatment for human papillomavirus-associated disease.



### AIMS

Most people experience human papillomavirus (HPV) infection during their lifetime but in some rare cases infection can cause cancers such as cervical, anal and head and neck cancers. Treatment is surgical removal of the precancers or cancers. Associated risks include sustained bleeding and for cervical precancers, preterm birth. This project set out to test whether a medical device that delivers mild microwave heating in a precise manner could have potential for treating precancers and cancers caused by HPV. We wanted to find out if microwave treatment could inhibit virus replication and inhibit cancer cell growth. For this study we used three dimensional "living skin" laboratory models of HPV-infected tissues.



### KEY FINDINGS

- Microwave treatment resulted in precise destruction of HPV-infected 3D tissues (representing precancers or cancers) without damage to surrounding areas.
- Levels of HPV proteins that are known to cause cancer formation was reduced.
- Immune pathways were activated.
- Microwave treatment reversed the appearance of the precancer and cancer tissues such that they displayed growth properties more similar to normal tissues.
- The localised cell death induced by microwave treatment was due to a normal cellular heat shock response.





## WHAT DID THE STUDY INVOLVE?

We developed a method to apply microwave treatment to laboratory-grown HPV-infected 3D tissues as models for HPV-associated precancers and cancers. We carried out precise temperature measurements to determine the optimum microwave energy required to elevate tissue temperature to the zone of efficacy (45-48°C) within a 7mm spatial zone. We used immunostaining to detect viral and cellular proteins that were affected by microwave treatment and observed microwave treatment effects up to six days following treatment.

A banner stand suitable for display in colposcopy clinics was designed to inform patients with HPV-associated disease of ongoing research. However, due to covid restriction, we were not able to deliver this patient-facing information. The study is progressing with a funded PhD student, Anna Kirk, and the banner stand will be utilised in clinics in 2024.

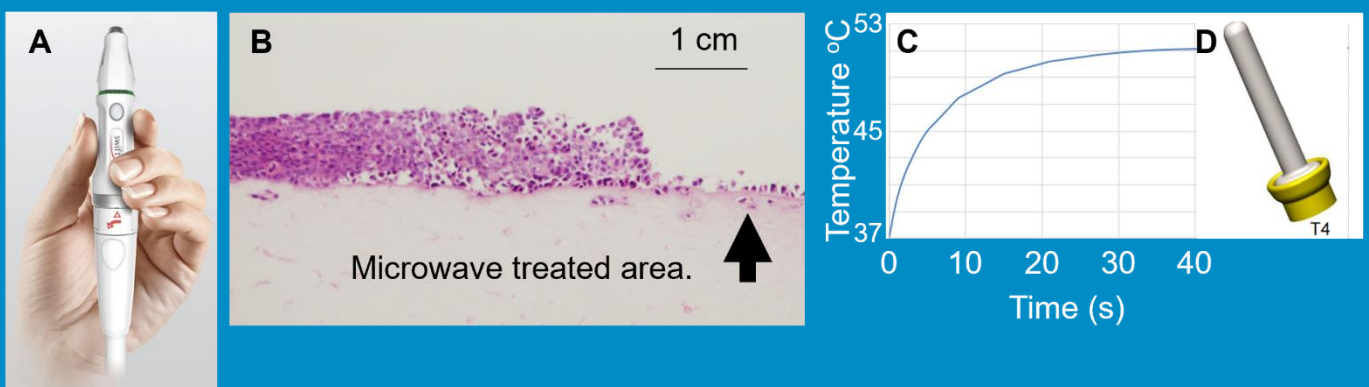


## WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Microwave treatment of tissues was localised to a 7 mm diameter area. Microwave treatment resulted in a reduction in tissue growth. Treated tissue areas did not regrow, even in the case of cancer tissues. The tissues representing precancers became much more normal in appearance after the use of microwave treatment. In summary:

- Microwave treatment reversed the cancer-like appearance of the treated tissues.
- Microwave treatment resulted in reduced levels of the HPV cancer-causing proteins (called HPV E6 and HPV E7).
- Microwave treatment triggered an immune response which would be predicted to clear virus infection.

Thus, microwave treatment inhibits cancer cell growth and allows the natural death process of HPV-infected cells to resume. Microwave treatment is precise and only transient delivery (10 seconds) is required. An anal precancer clinical trial planned for 2024 in Glasgow will show if patients tolerate the treatment and if it clears HPV-positive anogenital precancerous lesions and cancers without surgery.



A. The microwave device. B. Laboratory-grown cervical cancer tissue (stained purple) treated with the microwave device showing the area of destroyed tissue with only a few purple cells remaining. C. Graph of temperature increase upon microwave treatment. D. Different device head probes can be manufactured to fit different anatomical sites.



## WHAT IMPACT COULD THE FINDINGS HAVE?

- Current therapy for HPV-associated anogenital disease can cause sustained bleeding or inflammation.
- Heat treatment through microwaving could provide improved targeted tissue coverage and be more acceptable and better tolerated than existing strategies.
- The mild nature of the procedure would mean that sequential treatments could be spaced more closely and could save clinic time and resources.
- Recent increased incidence of HPV-associated anal, vulvar and penile cancers in Scotland means that easier, milder therapeutic approaches would be beneficial to these patients.



## HOW WILL THE OUTCOMES BE DISSEMINATED?

- Results are published in Lancet eBioMedicine at doi: 10.1016/j.ebiom.2023.104577.
- Project findings have been reported at the International Papillomavirus Conference 2022 and the DNA Tumour Virus Meeting 2022 to prompt discussions on future clinical uses.
- The University of Glasgow have disseminated information on the study to the media (e.g. article published in The Guardian: <https://www.theguardian.com/science/2023/may/18/microwave-device-could-be-less-invasive-treatment-for-hpv-caused-cancers>).
- With surgeons Miss Katrina Knight and Professor Campbell Roxburgh we have planned a clinical trial, supported by the Glasgow Clinical Trials Unit, to test the device and its acceptability on patients with HPV-associated anal precancers.



## CONCLUSION

- Microwaves can be delivered in a precise, highly localised manner.
- Microwaves stop cell growth and allow HPV-infected cells to die.
- Production of HPV cancer-causing proteins in treated tissues is reduced.
- Precision microwave delivery may present a potential new treatment for HPV-positive anogenital precancerous lesions and cancers (e.g. UK cervical cancer incidence >3,000, UK anal cancer >15,000 per annum.)



## RESEARCH TEAM & CONTACT

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### Additional Information

The project was completed on 31-03-2023. Funding was £299,914.

