Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report [1]

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number	TER503
Topic	Permanent implant brachytherapy devices for unresectable pancreatic cancer
Summary of findings	Pancreatic cancer is the 10th most common cancer in the UK and is most often diagnosed at an advanced stage where the tumour is unresectable. Permanent implant brachytherapy may be an effective adjunct to standard chemotherapy perfusion, leading to increased survival and resection rates. One health technology assessment, two systematic reviews, a meta-analysis, and one ongoing randomised controlled trial were identified. Study findings were mixed and seem to demonstrate improved outcomes in overall survival, resection rates and decreased pain. More comparative evidence is needed to assess the clinical effectiveness of the intervention when compared to standard practice.

[1] Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg
Translation of published technical HTW documents from English into Welsh

Introduction and aims

Pancreatic cancer is the 10th most common cancer in the UK – with around 10,500 people diagnosed each year (Cancer Research UK 2023). As pancreatic cancer is commonly diagnosed at a locally advanced (stage 3) or advanced stage (stage 4) it is often unresectable. Chemotherapy and radiotherapy are the main treatments for pancreatic cancer – with FOLFIRINOX (fluorouracil, irinotecan, oxaliplatin) chemotherapy being the most common treatment option.

Brachytherapy is a type of internal radiotherapy used to treat other forms of cancer and involves the implantation of radioactive material within the body to deliver a localised dose of radiotherapy to the affected area. Because it can be positioned precisely it minimises damage to healthy tissue. Brachytherapy may be an effective option for the treatment of locally advanced unresectable pancreatic cancer and in some cases could downstage disease making it suitable for potentially curative surgery. OncoSil was identified by the topic proposer as a specific example of this technology.

Health Technology Wales researchers searched for evidence on the effectiveness of permanent implant brachytherapy devices for the treatment of unresectable locally advanced pancreatic cancer.

Evidence overview

Guidance

No relevant guidance was identified.

Health Technology Assessments

An English-language summary of an Institute for Quality and Efficiency in Health Care (2022a) review on injection-based implantation of phosphorus-32 labelled microparticles for unresectable locally advanced pancreatic cancer was identified. The review identified 9 studies and concluded that there were no findings of benefit, ineffectiveness or harmfulness due to the lack of usable comparative data. An addendum to the review published later in 2022 (IQWiG 2022b) concluded that after further systematic review there was still no evidence of benefit, ineffectiveness or harmfulness of the technology and based on the completed and ongoing studies identified, it was unlikely that suitable evidence would be provided in the near future.

Systematic Reviews

A systematic review was undertaken as part of a clinical evaluation report conducted by OncoSil Medical (Turner et al, 2023) comparing the OncoSil phosphorus-32 microbrachytherapy device to standard care. The review identified 8 studies (n=4 from literature search, n=4 from internal sources). No randomised controlled trials were identified by the systematic review. Findings from one study identified by the systematic review suggest that OncoSil is effective in local disease control at 16 weeks (90.5% in the per protocol population), with a median overall survival rate of 15.5 months in the per protocol population. In the same study, 23.8% of patients underwent surgical resection with curative intent following OncoSil treatment, 80% of whom reached R0 margins. A single centre study identified by the review demonstrated that 50% of patients achieved tumour downstaging, with 42% having a successful resection and 33.3% of patients reaching R0 resection.

A systematic review by Willink, et al (2023) assessed intratumoral injection therapies for locally advanced pancreatic cancer. A total of 52 non-comparative studies were included in the review, of which 39 are relevant to this TER as they used iodine-125 seed brachytherapy (32 studies, 1283 patients), phosphorus-32 microbrachytherapy (5 studies, 133 patients) or palladium-103 seed brachytherapy (2 studies, 26 patients). The systematic review found that

Evidence overview

iodine-125 seed brachytherapy and palladium-103 seed brachytherapy were associated with low rates of complications (grade ≥3, iodine-125 risk 6.2%; palladium-103 risk 15%) while risk of developing the same complications with phosphorus-32 microbrachytherapy was higher (49.2%).

A meta-analysis by Han, et al (2017) studied the use of iodine-125 seed brachytherapy for unresectable pancreatic cancer (locally advanced to advanced) and measured outcomes relating to survival and pain relief. 23 non-comparative studies (total 824 patients) were included in the meta-analysis. Iodine-125 seed brachytherapy alone gave a pooled survival rate of 9-months (8.98, 95%CI 6.94-11.03), and the survival rate for iodine-125 seed implantation in combination with other therapies was approximately 12 months (11.75, 95%CI 9.84-13.65). The meta-analysis also notes that the majority of patients who underwent iodine-125 seed brachytherapy had their pain relieved.

Ongoing research

One ongoing multicentre randomised trial was identified comparing standard chemotherapy with chemotherapy plus phosphorus-32 brachytherapy (OncoSil) in patients with unresectable locally advanced pancreatic cancer (NLM, NCT05466799). This trial is due to complete in 2024.

Areas of uncertainty

- There appears to be limited comparative evidence for the use of brachytherapy implant devices in treating unresectable locally advanced pancreatic cancer.
- No Health Economic evidence was identified by HTW.
- One of the included systematic reviews mixed those with locally advanced and advanced disease. Aims of brachytherapy treatment would differ in these groups – being palliative in those with advanced disease but potentially curative in locally advanced disease.
- Whether permanent implant brachytherapy is currently used for the treatment of unresectable pancreatic cancer in Wales, and how it would integrate with current care pathways.
- In many of the studies brachytherapy treatment was combined with chemotherapy or chemoradiotherapy and it is unclear to what extent treatment complications relate to the brachytherapy component.
- Whether there is an important difference between the types of source (iodine-125, palladium-103 and phosphorus-32) used for brachytherapy treatment.

Literature search results

Health technology assessments and guidance
IQWiG. (2022). Endoscopic ultrasound-guided implantation via injection of 32P-labeled microparticles for unresectable, locally advanced pancreatic cancer. Available at: https://www.iqwig.de/download/h21-13_32p-labeled-microparticles-for-pancreatic-cancer_extract-of-137h-sgb-v-assessment_v1-0.pdf. IQWiG. (2022). Endoscopic ultrasound-guided implantation via injection of 32P-labeled microparticles for unresectable, locally advanced pancreatic cancer. Addendum to Commission H21-13.
Evidence reviews and economic evaluations
Willink CY, Jenniskens SFM, Klaassen NJM, et al. (2023). Intratumoral injection therapies for locally advanced pancreatic cancer: systematic review. BJS Open. 7(3). doi: 10.1093/bjsopen/zrad052 Han Q, Deng M, Lv Y, et al. (2017). Survival of patients with advanced pancreatic cancer after iodine125 seeds implantation brachytherapy: A meta-analysis. Medicine (Baltimore). 96(5): e5719. doi: 10.1097/MD.0000000000005719
Ongoing research
National Library of Medicine (U.S.). (2023, April – 2024, September). FOLFIRINOX Versus OncoSil™ in Addition to FOLFIRINOX in Patients With Locally Advanced Pancreatic Adenocarcinoma (TRIPP-FFX). Identifier NCT05466799. https://clinicaltrials.gov/study/NCT05466799
Evidence supplied by the topic proposer
Turner D, Tissing H, Gaddi N, et al. (2023). Clinical Evaluation Report OncoSil™ System (CER). Doc No.: REG_COMM_P_EMEA_011, revision 2. [Accessed 16 Oct 2023].
Reports
Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/pancreatic-cancer/incidence, [Accessed 16 October 2023].

Date of search	October 2023
Concepts used	Brachytherapy, pancreatic cancer, seed brachytherapy, intratumoral injection, LDR brachytherapy

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	What is the clinical and cost effectiveness of permanent implant brachytherapy devices for unresectable locally advanced pancreatic cancer?

	Inclusion criteria	**Exclusion criteria**
Population	Adults with unresectable pancreatic cancer	
Intervention	Permanent implant brachytherapy devices with or without chemotherapy or chemoradiotherapy	
Comparison/ Comparators	Chemotherapy or chemoradiotherapy	
Outcome measures	Local disease control, tumour downstaging, resection, Quality of life, overall survival, treatment related adverse events, outcomes relating to cost	

Proposed speciality	Cancer