NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **High dose rate brachytherapy using non-sealed rhenium for non-melanoma skin cancer (IP1975)**

Your information

Name:	Nicola Mulholland
Job title:	Consultant radiologist
Organisation:	King's College Hospital
Email address:	[redacted]
Professional organisation or society membership/affiliation:	BNMS
Nominated/ratified by (if applicable):	BNMS
Registration number (e.g. GMC, NMC, HCPC)	4203405

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

☐ Please tick this box if you would like to receive information about other NICE topics.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public

consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice.

x☐ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? – Is this procedure/technology performed/used by clinicians in specialities other than your own?	I am familiar with this technology. I have treated 22 patients and 37 lesions as part of EPIC trial, for which I am CI in UK. To date, I believe I am the only physician to have administered the activity in UK. It is not available yet in NHS. The procedure will be performed in radiation facilities compliant with legislation eg ARSAC, EA, IEMER, usually nuclear medicine physicians or clinical oncologists. Patient selection will be from dermatology and dermatooncology services. Speed of uptake will be constrained by product availability and suitably staffed radiation facilities. However, there is a very large population of potential suitable pts in view of the very common nature of non melanoma skin cancer

	– If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	. I have done clinical research on this procedure involving patients or healthy volunteers. .
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	The indication is appropriate. There is emerging evidence that other skin conditions which can be treated with radiotherapy eg Keloids may also be suitable, but evidence is more scant The technology of radiotherapy for NMSC is not novel at all and is established practise. The novelty of this treatment is the form of delivery of radiotherapy ie as high dose brachytherapy from unsealed rhenium 188. Definitely novel and of uncertain safety and efficacy.

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	It would be an addition to standard of care offering an effective alternative which patients may choose, particularly if unsuitable for first line standard of care ie Moh's surgery.
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	No

Current management

6	Please describe the current standard of care that is used in the NHS.	Current standard of care would be surgical excision if possible. Alternative treatments include radiotherapy, chemotherapy, topical treatments
7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	Conventional radiotherapy has similar mode of action. However, it requires multiple visits to radiotherapy suite which can make it unsuitable or unpalatable for patients eg frail pts. Patients commonly have multiple lesions which this treatment is able to treat at a single timepoint, unlike alternative of Moh's

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	Patients commonly have multiple lesions which this treatment is able to treat multiple cancers at a single timepoint, unlike the standard alternative of Moh's. It is better tolerated than surgery eg needle phobic and ther is no discomfort..
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Particularly suitable for frail patients, commonly elderly or with co morbidities, needle phobic pts. Also for patients with lesions in sites which are more challenging for surgery due to healing eg shins, or potentially more disfiguring/ complete eg nose, ears, face.
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	This therapy is less invasive than current SOC. It also involves fewer hospital visits. It could have potential to be delivered closer to home, eg in care homes for several pts in a single treatment as it is more portable
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Needs to be delivered in centres compliant with radiation protection governance. Commonly this is in hospitals already delivering open source therapy. A controlled area is required with a physician, technologist or nurse and medical physics expert available and appropriate waste facility.
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Relatively short additional training required for staff already used to handing open source brachytherapy

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:	Depigmentation of treated area (common), failure to work first time (97% lesions healed at 3/12 in EPIC trial). Late development of secondary malignancy is a theoretical complication of all bnrachytherapy eg decades later. Hence more suitable for older age groups.

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	Delayed wound healing, local alopecia, infection are uncommon. Radiation hazards – risk of contamination and unintended exposure (minimised with staff training)
14	Please list the key efficacy outcomes for this procedure/technology?	Rate of cure of NMSC Rate of recurrence Complication rate Patient experience
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Awaiting results of phase 4 trial.
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	It is not yet standard clinical care so there is uncertainty on impact on existing services for NMSC. It would be an second line treatment to improve patient and clinician choice
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Cannot predict at present.

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which	

	might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	EPIC trail
20	Please list any other data (published and/or unpublished) that you would like to share.	

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	I don't know
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post	Beneficial outcome measures: Adverse outcome measures:

	procedure timescales over which these should be measured:	

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	

NICE National Institute for Health and Care Excellence

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Non-financial professional	Chief investigator EPIC trial	**2022**	
Indirect			
Choose an item.			

x ☐ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Nicola Mulholland**
Dated:	**8.6.23**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **High dose rate brachytherapy using non-sealed rhenium for non-melanoma skin cancer (IP1975)**

Your information

Name:	Dr Shaunak Navalkissoor
Job title:	Consultant Nuclear Medicine Physician
Organisation:	Royal Free London NHS Foundation Trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	Royal College of Physicians; British Institute of Radiology; British Nuclear Medicine Society
Nominated/ratified by (if applicable):	British Nuclear Medicine Society
Registration number (e.g. GMC, NMC, HCPC)	GMC 4782649

How NICE will use this information:

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Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology?	I am familiar with this technology and have attended webinars/ read articles on its use
	Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? – Is this procedure/technology performed/used by clinicians in specialities other than your own?	No, as currently not funded. Not currently used in the NHS, it is used in clinical trials and a few private centres had looked to set this up. Technology is used in collaboration with nuclear medicine, clinical oncology and dermatology

	– If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. I have had no involvement in research on this procedure. Yes Other (please comment)
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Yes Established practice and no longer new. A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy. Definitely novel and of uncertain safety and efficacy. The first in a new class of procedure. x

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Yes, standard of care is usually surgery but surgery in patients with large or multiple lesions may lead to disfiguring scarring. In addition, surgery may be technically difficult in some areas e.g. digits, ears, eyes, nose. This procedure has potential to replace surgery in these scenarios.
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	No No guidance as yet

Current management

6	Please describe the current standard of care that is used in the NHS.	Surgical excision of non-melanoma skin cancer
7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	Similar efficacy as surgery with very good cosmetic results particularly in difficult surgical cases
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	As mentioned previously: patients with large or multiple lesions may lead to disfiguring scarring. In addition, surgery may be technically difficult in some areas e.g. digits, ears, eyes, nose.
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Potentially less invasive procedure in patients with large lesions.
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Existing nuclear medicine facility
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Visit of an established unit or proctoring by an established site.

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:	Skin burns, hair loss, infection, scarring, dermatitis, dry skin, skin ulceration, alopecia, skin induration, hypo/hyperpigmentation, and telangiectasia.

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	
14	Please list the key efficacy outcomes for this procedure/technology?	% of Complete response by visual analysis
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Long-term data recurrence data not available.
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	No
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Most or all district general hospitals. A minority of hospitals, but at least 10 in the UK. Y Fewer than 10 specialist centres in the UK. Cannot predict at present.

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent	Efficacy of Personalised Irradiation with Rhenium-Skin Cancer Therapy (SCT) for the treatment of non-melanoma skin cancer; a phase IV multi-centre, international, open label, single arm study. NCT05135052

	abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Not that I am aware.
20	Please list any other data (published and/or unpublished) that you would like to share.	

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Approximately 50% if patients with non melanoma skin cancer would potentially be eligible, but as surgery is an alternative, +- 10% of patients in total may have this as an altertnative
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: – Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. – Adverse outcome measures. These should include early and late complications. Please state the post	Beneficial outcome measures: QOL can be assessed by SKINDEX-16 QoL Questionnaire Comfort of Treatment and cosmetic outcomes can also be audited Adverse outcome measures: Safety (up to 24 months) Cosmetic Outcomes (12 months and 24 months)

	procedure timescales over which these should be measured:	

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	

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Declarations of interests

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Type of interest *	Description of interest	Relevant dates	
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Choose an item.			
Choose an item.			
Choose an item.			

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Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Click here to enter text. Shaunak Navalkissoor**
Dated:	**Click here to enter text. 16/5/23**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **High dose rate brachytherapy using non-sealed rhenium for non-melanoma skin cancer (IP1975)**

Your information

Name:	Stefan Adrian Voo
Job title:	Consultant Nuclear Medicine Physician
Organisation:	University College London Hospital
Email address:	
Professional organisation or society membership/affiliation:	British Nuclear Medicine Society
Nominated/ratified by (if applicable):	Ms. Caroline Oxley
Registration number (e.g. GMC, NMC, HCPC)	GMC 7550473

How NICE will use this information:

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Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? – Is this procedure/technology performed/used by clinicians in specialities other than your own?	I have evaluated the procedure for internal validation and usage at the UCLH for research and clinical purposes. I have summarised the evidence in the literature and prepared a systematic review on the topic of high dose topical epidermal brachyterapies, including Rhenium (article in preparation). I have reviewed the documentation prepared and submitted by the manufacturer (European branch) of the Rhenium compound (production, technical sheet, radiation protection). In addition, together with my molecular radionuclide therapy colleagues, I have consulted the application submitted by the manufacturer on Rhenium-188 brachytherapy for non-melanoma skin cancer to the Department of Health, Government of Australia and the detailed Assessment Report of the Medical Services Advisory Committee, affiliated to the Department of Health of the Australian Government. The detailed procedural information on the Rhenium product and therapy procedure is incorporated in the Report which I have submitted to the CESG committee UCL/UCLH for the introduction and use of Rhenium as a new interventional procedures. I have been trained in using the product (training provided/organised by the manufacturer in-line with EU requirements for provision of radionuclide therapies. I have obtained the ARSAC licence and permission to deliver the therapy.

	− If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Currently, the procedure is not used for NHS patients but provided only for private patients and in clinical research setting. The procedure is given by Nuclear Medicine physicians, but patients are referred to Nuclear Medicine by Dermatology or Radiation Oncology clinicians. After the therapy, patients are usually referred back to Dermatology (Dermato-oncology) and Radiation Oncology specialists for clinical follow-up.
2	− Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have prepared articles on this procedure (articles in preparation).
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Yes. Yes. There is evidence in the literature of similar products used for non-melanoma skin cancers. The Rhenium SCT compound is variation on a previous procedure. However, the newer compound is novel regarding its simplified methodology and a more rigorous way of dosing the radiation dose and effective dose to the tumoral lesion(s).
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Surgery remains the gold standard therapy for non-melanoma skin cancers. However, the Rhenium procedure is a feasible treatment alternative for a relatively large group of patients who would not be suitable to surgery or in which surgery would be mutilative and required secondary surgical reconstruction. Given in a single session therapy and having a high curative potential, Rhenium procedure is also a good alternative to conventional radiotherapy in patients with

		comorbidities which would not tolerate radiotherapy (given usually in >16 session over 1-2 months) or in which radiotherapy has a high risk of side effects.
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	No. No.

Current management

6	Please describe the current standard of care that is used in the NHS.	Curative surgery is the gold standard therapy in non-melanoma skin cancers. Conventional radiotherapy is an alternative to surgery.
7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	Electronic brachytherapy is also a novel effective therapeutic procedure, but it has a limited availability. Different mechanism of action. Given over multiple therapeutic sessions instead of a single therapy session in case of Rhenium. To my knowledge, there are no large clinical trials on the effectiveness of electronic brachytherapy.

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	Rhenium treatment is non-invasive, painless, can usually be delivered in a single session, over a short period of time (15 to 45 min, rarely up to 180 min), without the need for anaesthesia, in an outpatient setting, without functional mutilation or scarring and subsequent need for cosmetic repair. The relatively short healing time (usually within 30 days, rarely up to 120 days) and lack of aesthetic mutilation also mean a faster patient recovery and higher patient satisfaction compared to conventional therapies.
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Treatment will be particularly beneficial for lesions located on areas such as the nose, eyebrow, lip, ear, digit, genitalia, shin or collarbone, or for patients who are otherwise deemed unsuitable for treatment by surgery and/or external beam radiotherapy.
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Yes, definitely. Yes. Less costs for healthcare, less patient visits, limited side effects, very low recurrence rate. The net impact of these benefits for patients, in terms of no anaesthesia and very low infection risk, low procedural and post-operative pain, no disfiguration and scarring, health-related quality of life, low healthcare costs, and high functional and economic wellbeing are very significant aspects in favour of this new therapy. The reduced scarring and healing time mean also that patients can return to life sooner with no aesthetic harm and mutilation than would be expected after conventional treatment.
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Radiopharmacy and storage facility for radioactive compounds. Rhenium generator.
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes.

		The personnel delivering the therapy (Nuclear Medicine physicians) need to be trained, work under supervision (treatment of ~20 lesions), obtained ARSAC licence.

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	High radiation dose to healthy skin or tissue (e.g. eyes, mouth), in case the therapy is given by unexperienced professionals. Adverse events reported in the literature: wound bleeding, radiation dermatitis, mild skin discoloration at treatment site which is not painful or requires no further medical treatment. Hypothetical side effects could be skin redness, inflammation, bleeding, local infections, skin necrosis and excessive scar tissue/keloids.
14	Please list the key efficacy outcomes for this procedure/technology?	Better cosmesis and less side effects compared to standard therapies, while having comparable positive outcomes (high curative effect, low tumour recurrence rate).
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	None.
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	The price of the procedure may be a limiting factor. There are no other controversies about the procedure.
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	A minority of hospitals, but at least 10 in the UK.

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	BNMS webinar on Rhenium SCT (2021).
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Rhenium-188 SCT (OncoBeta) phase-3 trial (preliminary results are expected within months).
20	Please list any other data (published and/or unpublished) that you would like to share.	

1.	Retrospective cohort study	Cipriani et al, 2020: Personalised irradiation therapy for NMSC by rhenium-188 skin cancer therapy: a long-term retrospective study	Enrolled 52 patients with 55 confirmed NMSC lesions and included 12 months follow up. All lesions showed complete remission and no complications were reported.	pubmed.ncbi.nlm.nih.gov/32648530/	2020	IIb

		2.	Prospective observational cohort study	Castellucci et al, 2021: High dose brachytherapy with non-sealed 188 Re (rhenium) resin in patients with non-melanoma skin cancers (NMSCs): single centre preliminary results	Enrolled 50 patients with 60 confirmed NMSC lesions and included 24 months follow up. At 1 year all lesions were free from relapse and at 2 years a single relapse had occurred. Reported side effects were early, mild and resolved.	pubmed.ncbi.nlm.nih.gov/33140131/	2021	IIa
		3.	Retrospective cohort study	Carrozzo et al, 2014: Dermo Beta Brachytherapy with 188Re in extramammary Paget's disease	Enrolled 5 patients with EMPD and included 34 months of follow up. All lesions were healed after 1 or 2 treatment sessions. Reported side effects were early, mild and quickly resolved.	pubmed.ncbi.nlm.nih.gov/24566572/	2014	IIa
		4.	Prospective observational cohort study	Carrozzo et al, 2013: Dermo beta brachytherapy with 188-Re in squamous cell carcinoma of the penis: a new therapy	Enrolled 15 patients with SCC and included 51 months of follow up. Two patients (13%) did not respond to therapy.	pubmed.ncbi.nlm.nih.gov/23557628/	2013	Iia
		5.	Prospective observational cohort study	Sedda et al, 2008: Dermatological high-dose-rate brachytherapy for the treatment of basal and squamous cell carcinoma	Enrolled 53 patients with confirmed NMSC and included 51 months of follow up. All patients were in remission at 3 months and no relapses or other side effects were observed.	pubmed.ncbi.nlm.nih.gov/18681873/	2008	Iia
		6.	Retrospective cohort study	Cipriani et al, 2017: Personalised high-dose-rate brachytherapy with non-sealed Rhenium-188 in NMSC	Enrolled 43 patients with confirmed NMSC lesions and included 9.5 months follow up. All patients achieved and maintained remission.	www.cosmosscholars.com/special-issues-ijnmr/46-abstracts/ijnmr/737-abstract-	2017	IIa

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	156,000 new Non-melanoma skin cancer cases are being diagnosed and treated each year in UK. ~30% of patients would chose to be treated with Rhenium therapy instead of surgery or extensive radiotherapy.
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	Beneficial outcome measures: -cosmesis -curative rate -prognostic free survival -recurrence rate Adverse outcome measures: -local skin toxicity

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	There is need for further research, preferably head-to-head comparison with standard of care therapies.

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Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.	No conflict of interest.		
Choose an item.			
Choose an item.			

☒ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Dr. Stefan Adrian Voo**
Dated:	**05/06/2023**

View results

Respondent

4 Anonymous

79:48
Time to complete

1. Project Number and Name - (Can be found on email) *

IP1975

Your information

2. Name: *

Agata Rembielak

3. Job title: *

Consultant Clinical Oncologist

4. Organisation: *

The Christie NHS Foundation Trust and The University of Manchester

5. Email address: *

agata.rembielak@nhs.net

6. Professional organisation or society membership/affiliation: *

RCR

7. Nominated/ratified by (if applicable):

Dr Tom Roques, RCR Vice President for Clinical Oncology

8. Registration number (e.g. GMC, NMC, HCPC) *

GMC 6159837

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice: https://www.nice.org.uk/privacy-notice

9. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

10. Please describe your level of experience with the procedure/technology, for example:

Are you familiar with the procedure/technology?

I am a clinical oncologist with special interest in skin cancers. I have many years of experience in skin radiotherapy (various techniques) and am a director on ESTRO skin course.
I am familiar with the technology, its rationales and logistics of application together with results of clinical studies conducted so far. I have not treated patients myself as King's College was the only site in the UK to conduct the EPIC-Skin study. Potential uptake would depend on how many sites in UK are able to offer such tretament.

11. Have you used it or are you currently using it?

- Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

- Is this procedure/technology performed/used by clinicians in specialities other than your own?

- If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.

Within UK I am aware of the EPIC-Skin phase 4 clinical trial run at the one NHS site King's College Hospital.
The procedure requires multidisciplinary team with involvement from dermatology, nuclear medicine and clinical oncology specialities.
As King's College London is the only site providing such treatment I have not referred patients from North West.

12. Please indicate your research experience relating to this procedure (please choose one or more if relevant):

- [x] I have done bibliographic research on this procedure.
- [x] I have done research on this procedure in laboratory settings (e.g. device-related research).
- [ ] I have done clinical research on this procedure involving patients or healthy volunteers.
- [ ] I have published this research.
- [ ] I have had no involvement in research on this procedure.
- [x] I teach on ESTRO skin course and also authored

13. Does the title adequately reflect the procedure?

- ( ) Yes
- (•) High dose rate (HDR) brachytherapy traditionally

14. Is the proposed indication appropriate? If not, please explain

yes but it would be helpful to detailed what NMSC are regarded as appropriate indications eg BCC only or all keratinocyte tumours, any rare skin cancers?

15. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

The concept of superficial application is not new as used also in PDT and alpha emitters for superficial skin cancer. The novel approach is to provide beta radiation in the form of a paste applied directly to the skin.

16. Which of the following best describes the procedure:

- ( ) Established practice and no longer new.
- ( ) A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.
- (•) Definitely novel and of uncertain safety and efficacy.
- ( ) The first in a new class of procedure.

17. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

In my opinion this procedure would be used as an addition to existing standard care but would definitely widen the scope of treatments we can offer to patients with skin cancer

Current management

18. Please describe the current standard of care that is used in the NHS.

The standard of care within NHS has been published by UK BAD in their recent guidelines for BCC and cSCC. It depends on initial presentation of skin cancer and involves dermatology treatments, surgery, radiotherapy, systemic treatment or combination.

19. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

    At the moment I am not aware of any competing non sealed radiation procedure to compete directly with the rhenium paste for skin cancer. For the same group of patients other non-surgical treatments are used, including topical /dermatology treatments, PDT or skin radiotherapy (sealed sources).

Potential patient benefits and impact on the health system

20. What do you consider to be the potential benefits to patients from using this procedure/technology?

    One-off application
    The biggest limitation for this technique is the depth of range for radiation and would include predominantly patients with very superficial skin cancers

21. Are there any groups of patients who would particularly benefit from using this procedure/technology?

    It could be of benefit to older / frail patients that may not be able to attend hospital appointments on multiple occasions

22. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

    Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

    It can definitely reduced number of hospital visits

23. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

    As this is an open source its application requires close cooperation between nuclear medicine (expertise with open sources), clinical oncology / radiotherapy team (expertise in localised radiation based treatment with sealed sources) and dermatology (expertise in skin cancer). Such set up would require changes to existing facilities.

24. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

    Yes and that includes training on usage of open sealed radiation for localised skin application

Safety and efficacy of the procedure/technology

25. What are the potential harms of the procedure/technology?

    Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

    - Adverse events reported in the literature (if possible, please cite literature)
    - Anecdotal adverse events (known from experience)
    - Theoretical adverse events

    Toxicity profile is similar to the one that we see in skin radiotherapy
    As the technique is new and was introduced relatively recently there is limited literature evidence on long term toxicity (cosmesis, secondary malignancy in the treated area).

26. Please list the key efficacy outcomes for this procedure/technology?

As the technique is new and was introduced relatively recently there is limited literature evidence on long term efficacy.

27. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

The manufacturer states that the technique is applicable for skin lesions up to 3 mm depth. What imaging can be used to guide our decision? It in unclear whether this 3 mm cut off is including the deep margin for possible microinfiltration from skin cancer. It is also unclear what margins need to be applied around the visible skin lesions and would they need to be different for different subtypes or sizes of skin cancer.

28. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

Please see the above

29. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- ○ Most or all district general hospitals.
- ◉ A minority of hospitals, but at least 10 in the UK.
- ○ Fewer than 10 specialist centres in the UK.
- ○ Cannot predict at present.

Abstracts and ongoing studies

30. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

There is a relatively big amount of publications freely available on internet.

31. Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.

EPIC-Skin clinical trial is registered on clinicaltrials.gov website

32. Please list any other data (published and/or unpublished) that you would like to share.

Rhenium technology has also been used in keloids (non-cancer skin conditions) https://pubmed.ncbi.nlm.nih.gov/28621443/

Other considerations

33. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

It is very difficult to provide an estimate at this stage but BCC is the most common cancer in adults and its incidence is rapidly rising worldwide. The trends in keratinocyte tumours incidence has been recently published in BJD https://pubmed.ncbi.nlm.nih.gov/36763862/

34. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

short and long term side effects (within 3-6 months after application and from 6 months onwards)
QoL
PROMs
It is very important to include patients representatives in such work.

35. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

skin necrosis, secondary cancer in the treated area, permanent depigmentation, permanent hair loss - chronic toxicity measure from 6 months onwards after application

Further comments

36. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

radiation protection
required licensing in UK ?covered by ARSAC/requirement for new ARSAC applications for existing holders that would treat with beta emitters

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

37. Type of interest: *

- [ ] Direct: financial
- [ ] Non-financial: professional
- [ ] Non-financial: personal
- [ ] Indirect
- [x] No interests to declare

38. Description of interests, including relevant dates of when the interest arose and ceased. *

No interests to declare

39. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website. *

- (●) I agree
- ( ) I disagree

Signature

40. Name: *

Agata Rembielak

41. Date: *

19/05/2023