



Australian Government

Department of Health

Application Form

Cryoablation for small renal mass

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au

Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):

Corporation name: Boston Scientific/BTG International Asia Limited (Australian distributor is Big Green)

ABN: REDACTED

Business trading name: REDACTED

Primary contact name: REDACTED

Primary contact numbers

Business: REDACTED

Mobile: REDACTED

Email: REDACTED

Alternative contact name: REDACTED Alternative contact numbers

Business: REDACTED

Mobile: REDACTED

Email: REDACTED

2. (a) Are you a lobbyist acting on behalf of an Applicant?

Yes

No

(b) If yes, are you listed on the Register of Lobbyists?

Yes

No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Cryoablation for small renal masses

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Small masses in the kidney are considered to be cancerous until proven otherwise. Renal cell carcinoma (RCC; cancer that starts in cells that line the tubules of the kidney) is the most common type of kidney cancer. Risk factors for developing RCC include older age (> 64 years), gender (twice as common in men), obesity, high blood pressure, and smoking. Due to the increased use of cross-sectional imaging, a growing number of renal tumours are incidentally discovered at earlier stages which increases the chance of treatment success. Renal cancer is stratified into 4 stages (I-IV). Stage I is defined as tumor size up to 7 centimetres in diameter, that is confined to the kidney. Tumours measuring ≤ 4 cm are considered small renal masses (Stage 1a) and are the subject of this application.

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

Cryoablation (also known as cryotherapy or cryosurgery) is a well-established technology for the treatment of many benign and malignant tumours and lesions. Cryoablation destroys tissue by freezing the cancer cells. Very precise targeting and control of the extremely cold energy allow for efficient destruction of tumor cells while leaving healthy kidney tissue intact and functional.

To freeze the cancer, special ultra-thin probes called cryoablation needles are inserted into the site targeted for ablation. Argon gas is delivered under pressure into a small chamber inside the tip of the needle where it expands and cools, reaching a temperature well below -100° Celsius. This produces an iceball of predictable size and shape around the needle. This iceball engulfs the tumor, killing the cancerous cells as well as a small margin of surrounding tissue while sparing healthy kidney structures. A number of approaches can be used to perform renal cancer cryoablation, so the physician can customise the treatment to accommodate the patient's general health as well as the size and location of the tumor. A minimally invasive approach (either percutaneous or laparoscopic), rather than an open surgical approach, is usually preferred.

6. (a) Is this a request for MBS funding?

- Yes
 No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

- Amendment to existing MBS item(s)
 New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

Not applicable

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

- i. An amendment to the way the service is clinically delivered under the existing item(s)
- ii. An amendment to the patient population under the existing item(s)
- iii. An amendment to the schedule fee of the existing item(s)
- iv. An amendment to the time and complexity of an existing item(s)
- v. Access to an existing item(s) by a different health practitioner group
- vi. Minor amendments to the item descriptor that does not affect how the service is delivered

- vii. An amendment to an existing specific single consultation item
- viii. An amendment to an existing global consultation item(s)
- ix. Other (please describe below):

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

- i. A new item which also seeks to allow access to the MBS for a specific health practitioner group
- ii. A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
- iii. A new item for a specific single consultation item
- iv. A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

- Yes
- No

(g) If yes, please advise:

Not applicable

7. What is the type of service:

- Therapeutic medical service
- Investigative medical service
- Single consultation medical service
- Global consultation medical service
- Allied health service
- Co-dependent technology
- Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service (which could be one or more of the following):

Not applicable

- i. To be used as a screening tool in asymptomatic populations
- ii. Assists in establishing a diagnosis in symptomatic patients
- iii. Provides information about prognosis
- iv. Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
- v. Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

- Pharmaceutical / Biological
- Prosthesis or device
- No

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

Not applicable

(b) If yes, please list the relevant PBS item code(s):

Not applicable

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

Not applicable

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Not applicable

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

Not applicable

(b) If yes, please provide the following information (where relevant):

Not applicable

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

Not applicable

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

There is one additional general cryosurgical system listed on the ARTG (ARTG no. 308786). The Sponsor of this device is Surgeons Choice Australia Pty Ltd and the Manufacturer is IceCure Medical Ltd. It is BTG's understanding that this unit is not being used for this indication in Australia.

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

Not applicable

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Multi-use consumables:

- Visual-ICE Cryoablation System

Single use consumables:

- The following accessories to the Visual-ICE System are single use only:
 - Galil Medical Cryoablation Needles

* Note: The following items are needed to conduct cryoablation procedures and are not available from Galil Medical:

- Argon gas cylinder(s)
- Helium gas cylinder(s) if using helium for thawing
- Sterile drape to cover touch screen if system operated by members of the sterile team

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: 45738 Electronic general cryosurgical system
Manufacturer's name: Galil Medical Inc¹
Sponsor's name: Big Green Surgical Company Pty Ltd

Type of therapeutic good: 45140 Cryotherapy set
Manufacturer's name: Galil Medical Inc¹
Sponsor's name: Big Green Surgical Company Pty Ltd

*In the Cryotherapy for Recurrent Prostate Cancer and Renal Cancer Assessment Report (MSAC 2009), a "cryosurgical unit, general purpose" from Scanmedics Pty Ltd is noted (ARTG no. 144069). This unit is no longer listed on the ARTG.

- (b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

- Class III
 AIMD
 N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

- Yes (If yes, please provide supporting documentation as an attachment to this application form)
 No

- (b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

- Yes (if yes, please provide details below)
 No

ARTG listing, registration or inclusion number: 221468 – Electronic general cryosurgical system
TGA approved indication(s), if applicable: Not applicable
TGA approved purpose(s), if applicable: The Visual-ICE Cryoablation System is intended for cryoablative destruction of tissue during minimally invasive, transient surgical procedures. The System is indicated for use as a cryosurgical tool in the fields of general surgery, dermatology, neurology, thoracic surgery, ENT, gynaecology, oncology, proctology, and urology. This system is designed to destroy tissue (including prostate and kidney tissue, liver metastases, tumours, skin lesions, and warts) by the application of extremely cold temperatures.

ARTG listing, registration or inclusion number: 224583 – cryotherapy set
TGA approved indication(s), if applicable: Not applicable
TGA approved purpose(s), if applicable: Procedure packs containing cryoablation needles and accessories intended to be used with a cryoablation system for the destruction of tissue during minimally invasive, transient surgical procedures.

Also, see Q11d.

¹ Galil Medical is a BTG Company.

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

Not applicable

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

Not applicable

PART 4 – SUMMARY OF EVIDENCE

17. Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only). Please do not attach full text articles, this is just intended to be a summary.

Three comparators are considered relevant to this application: two main comparators (active surveillance/deferred therapy and radiofrequency ablation) and one supplementary comparator (partial nephrectomy). Justification for these comparators is provided in PART 6c of this Application.

Main comparator 1 – Active surveillance/deferred therapy

No meta-analyses and three individual comparative studies (Table 1) were identified as being relevant to the comparison between cryoablation and active surveillance/deferred therapy for the treatment of small renal mass/RCC.

Table 1 Individual studies comparing cryoablation/thermal ablation with active surveillance/deferred therapy for the treatment of small renal mass or renal cell carcinoma

#	Type of study design ²	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)	Website link to journal article or research (if available)	Date of publication
-	Cryoablation vs active surveillance/deferred therapy studies	-	-	-	-
-	<i>Matched population or analysis adjusted for confounding</i>	-	-	-	-
1	Retrospective cohort SEER database, US 2000 to 2013	Treatment for Localized T1a Clear Cell Renal Cell Carcinoma: Survival Benefit for Cryosurgery and Thermal Ablation Compared to Deferred Therapy	Patients with histopathologically-confirmed localised T1a clear cell RCC who received CA (N=315), RFA (N=155) or DT (N=263) Cancer-specific survival outcome analysis adjusted	https://www.ncbi.nlm.nih.gov/pubmed/29075878	Uhlig 2018

² Studies are ordered in reverse chronological order. Where studies are from the same centre they are grouped together.

#	Type of study design ²	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)	Website link to journal article or research (if available)	Date of publication
2	Prospective cohort DISSRM registry, US Jan 2009 to Aug 2013	Active Surveillance is Superior to Radical Nephrectomy and Equivalent to Partial Nephrectomy for Preserving Renal Function in Patients with Small Renal Masses: Results from the DISSRM Registry	Patients with small renal masses who elect AS (N=68), RN, PN or CA (N=14) CKD upstaging-free survival outcome; adjusted for various demographic and disease characteristics	https://www.ncbi.nlm.nih.gov/pubmed/25813449	Danzig 2015
-	Thermal ablation vs active surveillance/deferred therapy studies	-	-	-	-
-	<i>Matched population or analysis adjusted for confounding</i>	-	-	-	-
3	Retrospective cohort SEER–Medicare-lined database, US 2002 to 2012	Comparative Effectiveness of Thermal Ablation, Surgical Resection, and Active Surveillance for T1a Renal Cell Carcinoma: A Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked Population Study	Patients with T1aN0M0 RCC who underwent PN, RN, AS (N=647) or CA (N=647) Overall survival and cancer-specific survival outcomes; populations propensity score-matched based on 17 demographic and disease characteristic variables	https://www.ncbi.nlm.nih.gov/pubmed/29737950	Xing 2018

Abbreviations: AS, active surveillance; CA, cryoablation; DISSRM, Delayed Intervention and Surveillance for Small Renal Masses; DT, deferred therapy; PN, partial nephrectomy; RCC, renal cell carcinoma; RFA, radiofrequency ablation; RN, radical nephrectomy; SEER, Surveillance, Epidemiology and End Results.

Main comparator 2 – Radiofrequency ablation

One meta-analysis (Table 2) and 18 individual comparative studies (Table 3) were identified as being relevant to the comparison between cryoablation and radiofrequency ablation for the treatment of small renal mass/RCC.

Comparison with radiofrequency ablation for the treatment of small renal mass or renal cell carcinoma

Journal article or project (including identifier or study variant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
Nephrectomy versus ablation techniques for small renal masses: a systematic review and network meta-analysis	<p>Meta-analysis of data from 47-comparative studies.</p> <p>Assessed all-cause mortality, cancer-specific mortality, local recurrence, complications and renal function.</p> <p>Used network meta-analysis to compare treatments. Used adjusted results where available. Survival and oncological outcomes calculated per patient month using follow-up duration.</p>	<p>https://www.ncbi.nlm.nih.gov/pubmed/30255245</p>	Uhlir 2019

Comparison with radiofrequency ablation for the treatment of small renal mass or renal cell carcinoma

Journal article or project (including identifier or study variant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
	-	-	-

#	Type of study design ⁴	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
1	Retrospective cohort Mayo Clinic, US 2000 to 2011 ⁵	Oncologic outcomes following partial nephrectomy and percutaneous ablation for cT1 renal masses	Patients with sporadic, localised cT1 (a or b) masses who received treatment with PN (N=1055), CA (N=187) or RFA (N=180) Analyses of overall survival and cancer-specific survival propensity score-adjusted for various demographic and disease characteristics. T1a and T1b masses considered separately. No head to head comparison between CA and RFA conducted; CA and RFA will be compared indirectly via PN.	https://www.ncbi.nlm.nih.gov/pubmed/31060824	Andrews 2019
2	Retrospective cohort SEER database, US 2000 to 2013	Treatment for Localized T1a Clear Cell Renal Cell Carcinoma: Survival Benefit for Cryosurgery and Thermal Ablation Compared to Deferred Therapy	Patients with histopathologically-confirmed localised T1a clear cell RCC who received CA (N=315), RFA (N=155) or deferred therapy (N=263) Cancer-specific survival outcome analysis adjusted	https://www.ncbi.nlm.nih.gov/pubmed/29075878	Uhlig 2018
3	Retrospective cohort Tufts University, US Oct 2006 to Oct 2016	Thermal Ablation of T1c Renal Cell Carcinoma: A Comparative Assessment of Technical Performance, Procedural Outcome, and Safety of Microwave Ablation, Radiofrequency Ablation, and Cryoablation	Patients with biopsy-proven T1N0M0 RCC who underwent PCA (N=41), PRFA (N=305) or PMWA (N=38) Complications and residual disease outcome analyses adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/29628298	Zhou 2018

⁵ Same centre, timeframe and outcomes as Thompson 2015, but analyses are adjusted for potential confounding.

#	Type of study design ⁴	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
-	<i>Analysis not adjusted for confounding</i>	-	-	-	-
4	Retrospective cohort Emory University School of Medicine, US Jan 2008 to Sep 2013	R.E.N.A.L. (Radius, exophytic/endophytic, nearness to collecting system or sinus, anterior/posterior, and location relative to polar lines) nephrometry score predicts early tumor recurrence and complications after percutaneous ablative therapies for renal cell carcinoma: a 5-year experience	Patients with biopsy-proven RCC who underwent PCA (N=47) or PRFA (N=40) Recurrence and complications outcomes; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/25769213	Camacho 2015
5	Retrospective cohort Mayo Clinic Jun 2001 to May 2012 ⁶	Percutaneous Clinical T1a Renal Mass Ablation in the Octogenarian and Nonagenarian: Oncologic Outcomes and Morbidity	Patients aged ≥ 80 years who underwent PCA (N=61) or PRFA (N=44) for T1a renal mass Oncologic, survival, renal and perioperative outcomes; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/25386995	Miller 2015
6	Retrospective cohort (prospective registry) Mayo Clinic, US 2000 to 2011 ⁷	Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses	Patients treated with PN (N=1057), RFA (N=180) or PCA (N=187) for sporadic, localised cT1 solid renal masses Comparison between CA and RFA not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/25108580	Thompson 2015
7	Retrospective cohort Mayo Clinic, US 2000 to 2010 ⁸	Percutaneous ablation of renal masses measuring 3.0 cm and smaller: comparative local control and complications after radiofrequency ablation and cryoablation	Renal masses measuring ≤ 3 cm treated with CA (N=189) or RFA (N=256) Local control and complications outcomes; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/23345372	Atwell 2013

⁶ May be some overlap with other Mayo Clinic studies but population limited to patients aged ≥ 80 years.

⁷ Same centre, timeframe and outcomes as Andrews 2019, but analyses are not adjusted for potential confounding.

⁸ Same centre, timeframe and similar outcomes to Atwell 2012, but analysis limited to tumours ≤ 3cm.

Journal article or project (including identifier or study variant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
Patients following 573 percutaneous renal mass ablation procedures	Patients treated with renal RFA (N=254) and CA (N=311) Complications; analyses not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/22037491	Atwell 2012
Patients following 100 percutaneous computed tomography-guided renal mass ablation versus open surgery: doses of sedation used	Patients who underwent PCA (N=65) or PRFA (N=71) for small renal mass Sedation medication dosing; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/23433410	Truesdale 2013
Patients following 100 percutaneous thermal ablation procedures in patients with pre-existing chronic kidney disease	Patients with baseline CKD (GFR < 60 mL/min/1.73m ²) who underwent PCA (N=22) or PRFA (N=26) for renal masses Renal function outcomes; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/22019179	Wehrenberg-Klee 2012
Patients following 100 percutaneous ablation for renal masses in 65 solitary kidneys: functional and oncological outcomes	Patients with a solitary kidney who underwent CA (N=29) or RFA (N=36) for renal masses Functional and oncological outcomes; analyses not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/21571336	Altunrende 2011
Patients following 100 minimally-invasive nephron-sparing management for renal masses in solitary kidneys	Patients who underwent LPN (N=36), CA (N=36) or RFA (N=29) for tumours in a <u>solitary kidney</u> Functional and oncological outcomes. Comparison between CA and RFA not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/19758655	Turna 2009

#	Type of study design ⁴	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
13	Retrospective cohort 2 centers, US ¹² 2006 to 2009	Cryoablation vs. radiofrequency ablation for small renal masses	Patients who underwent PCA (N=70) or PRFA (N=41) for suspected RCC Recurrence and complications outcomes; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/20880723	Pirasteh 2011
14	Retrospective cohort University of Wisconsin, US Oct 2000 to Jun 2006	Comparison of postoperative pain, convalescence and patient satisfaction between laparoscopic and percutaneous ablation of small renal masses	Patients who underwent LCA (N=58), PCA (N=20) or PRFA (N=15) for small renal masses Perioperative outcomes; analyses not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/18643721	Bandi 2008
15	Retrospective cohort 7 institutions, US ¹³ Timeframe NR	Residual and recurrent disease following renal energy ablative therapy: a multi-institutional study	Patients who underwent CA (N=206) or RFA (N=410) for small renal mass Survival and recurrent disease outcomes; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/17070224	Matin 2006
16	Retrospective cohort Johns Hopkins Medical Institutions, US Jun 2003 to Feb 2004	Pain control requirements for percutaneous ablation of renal tumours: cryoablation versus radiofrequency ablation – initial observations	Patients who underwent PRFA (N=14) or PCA (N=10) for renal tumours Analysis of pain control dosing requirements (midazolam or fentanyl) – analyses not adjusted for confounding	https://www.ncbi.nlm.nih.gov/pubmed/16126920	Allaf 2005
17	Retrospective cohort 4 institutions, US ¹⁴	Defining the complications of cryoablation and radio frequency ablation of small renal tumors: a multi-institutional review	Patients treated for small renal tumours using CA (N=139) and RFA (N=132) Complications; not adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/15310987	Johnson 2004

¹² University Hospitals Case Medical Center, Metrohealth Medical Center

¹³ University of Texas M. D. Anderson Cancer Center, University of Texas Southwestern Medical Center, Massachusetts General Hospital, Wake Forest University Baptist Medical Center, Fox Chase Cancer Center, Case Western Reserve University, Cleveland Clinic

¹⁴ University of Utah Health Sciences Center, Brady Urological Institute, University of Wisconsin Hospitals and Clinics, University of Wisconsin and Veterans Administration Medical Center, University of Mississippi Medical Center, University of Texas Southwestern Medical Center

Abbreviations: CA, cryoablation; LCA, laparoscopic cryoablation; LRFA, laparoscopic radiofrequency ablation; PRFA, percutaneous radiofrequency ablation; PCA, percutaneous cryoablation; RCC, renal cell carcinoma; RFA, radiofrequency ablation; US, United States of America.

Supplementary comparator – Partial nephrectomy

Four meta-analyses (Table 4) and 18 individual comparative studies that included matched populations or adjusted for potential confounding (Table 5) were identified as being relevant to the comparison between cryoablation and partial nephrectomy for the treatment of small renal mass/RCC. Due to the large number of studies with matched populations/adjusted analyses, additional studies with non-adjusted analyses will likely not be required.

Table 4 Meta-analyses comparing cryoablation with radiofrequency ablation for the treatment of small renal mass or renal cell carcinoma

#	Type of study design ¹⁵	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
1	Meta-analysis	Cryoablation versus Partial Nephrectomy for Clinical Stage T1 Renal Masses: A Systematic Review and Meta-Analysis	Meta-analysis of data from 17 retrospective comparative studies Assessed all-cause death, cancer-specific death, metastasis, local recurrence, renal function and complications outcomes. All included studies had groups that were matched or comparable for at least one variable (tumour location) and up to nine variables).	https://www.ncbi.nlm.nih.gov/pubmed/30854132	Deng 2019
2	Network meta-analysis	Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis	Meta-analysis of data from 47 comparative studies. Assessed all-cause mortality, cancer-specific mortality, local recurrence, complications and renal function. Used network meta-analysis to compare treatments. Used adjusted results where available. Survival and oncological outcomes calculated per patient month using follow-up duration.	https://www.ncbi.nlm.nih.gov/pubmed/30255245	Uhlig 2019
3	Meta-analysis	Systematic review and meta-analysis of perioperative and oncologic outcomes of laparoscopic cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal tumors	Meta-analysis of data from 13 retrospective comparative studies Assessed perioperative and oncologic outcomes Used raw data from included studies; no adjustment for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/24231845	Klatte 2014

¹⁵ Studies are ordered in reverse chronological order. Where studies are from the same centre they are grouped together.

#	Type of study design ¹⁵	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
4	Meta-analysis	Laparoscopic renal cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal masses: a systematic review and meta-analysis of comparative studies	Meta-analysis of data from nine retrospective comparative studies Assessed perioperative and oncologic outcomes Used raw data from included studies; no adjustment for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/24914926	Tang 2014

Table 5 Individual studies comparing cryoablation with partial nephrectomy for the treatment of small renal mass or renal cell carcinoma

#	Type of study design ¹⁶	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
-	<i>Matched population or analysis adjusted for confounding</i>	-	-	-	-
1	Retrospective cohort Mayo Clinic, US 2000 to 2011 * Likely to be some overlapping patients between Mayo Clinic studies	Oncologic outcomes following partial nephrectomy and percutaneous ablation for cT1 renal masses	Patients with sporadic, localised cT1 (a or b) masses who received treatment with PN (N=1055), CA (N=187) or RFA Analyses of overall survival and cancer-specific survival propensity score-adjusted for various demographic and disease characteristics. T1a and T1b masses considered separately. No head to head comparison between CA and RFA conducted; CA and RFA will be compared indirectly via PN.	https://www.ncbi.nlm.nih.gov/pubmed/31060824	Andrews 2019

¹⁶ Studies are ordered in reverse chronological order. Where studies are from the same centre they are grouped together.

#	Type of study design ¹⁶	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
2	Retrospective cohort Mayo Clinic, US 2005 to 2015	Outcomes After Cryoablation Versus Partial Nephrectomy for Sporadic Renal Tumors in a Solitary Kidney: A Propensity Score Analysis	Patients who underwent PN (N=64) or CA (N=54) for a single noncystic renal tumour in a solitary kidney Complications, renal outcomes, oncologic outcomes and mortality outcomes; used ITPW weighting to adjust for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/28967553	Bhindi 2018
3	Retrospective cohort Mayo Clinic, US 2003 to 2013	Renal functional outcomes in patients undergoing percutaneous cryoablation or partial nephrectomy for a solitary renal mass	Patients treated with PCA (N=481) or PN (N=1650) for a unilateral, solitary renal mass Propensity score matched (389 each group); also reweighting via inverse probability weights (PCA=410; PN=1,598) Analysis of renal function	https://www.ncbi.nlm.nih.gov/pubmed/28548236	Mason 2017
4	Retrospective cohort (prospective registry) Mayo Clinic, US 2000 to 2011	Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses	Patients treated with PN (N=1057), RFA (N=180) or PCA (N=187) for sporadic, localised cT1 solid renal masses Overall survival outcome adjusted	https://www.ncbi.nlm.nih.gov/pubmed/25108580	Thompson 2015
5	Retrospective cohort Cleveland Clinic, US Jun 2006 to Dec 2016 * Likely to be some overlapping patients between Cleveland Clinic studies	Perioperative, oncological and functional outcomes after robotic partial nephrectomy vs. cryoablation in the <u>elderly</u> : A propensity score matched analysis	Review of 312 consecutive elderly patients (> 75 years) with a renal mass who underwent PN or CA Propensity score matching of 130 patients (65 from each group) Analysis of perioperative and postoperative outcomes, renal function and oncological/survival outcomes	https://www.ncbi.nlm.nih.gov/pubmed/30691958	Bertolo 2019

#	Type of study design ¹⁶	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
6	Retrospective cohort Cleveland Clinic, US Dec 2000 to Jan 2012 * Likely to be some overlapping patients with Turna 2009 and Guillotreau 2012	Cryoablation versus minimally invasive partial nephrectomy for small renal masses in the <u>solitary kidney</u> : impact of approach on functional outcomes	Review of 111 patients with a solitary functioning kidney who underwent CA (N=59) or PN (N=52) Grouped based on RENAL nephrometry score Analysis of peri- and postoperative outcomes and renal function	https://www.ncbi.nlm.nih.gov/pubmed/23009872	Panumatrassamee 2013
7	Retrospective cohort Cleveland Clinic, US Jan 1998 to Dec 2010 * Likely to be some overlapping patients with Turna 2009	Robotic partial nephrectomy versus laparoscopic cryoablation for the small renal mass	Patients with small renal masses (≤ 4 cm) treated with RPN (N=210) or LCA (N=226) Complications and eGFR outcomes analyses adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/22264680	Guillotreau 2012
8	Retrospective cohort Cleveland Clinic, US Sep 1997 to Oct 2006	Minimally invasive nephron sparing management for renal tumors in <u>solitary kidneys</u>	Patients who underwent LPN (N=36), CA (N=36) or RFA (N=29) for tumours in a solitary kidney Renal function outcome analyses adjusted	https://www.ncbi.nlm.nih.gov/pubmed/19758655	Turna 2009
9	Retrospective cohort France 2009 to 2016	Peri-operative and local control outcomes of robot-assisted partial nephrectomy vs percutaneous cryoablation for renal masses: comparison after matching on radiological stage and renal score	Review of all patients with localised renal tumour treated by RPN (N=470) or PCA (N=177) for malignant renal tumours in one of four centres Matching of 354 patients (177 in each group) for recurrence outcomes only. Local recurrence outcome multivariate analysis also adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/30153399	Fraisse 2019

#	Type of study design ¹⁶	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
10	Retrospective cohort National Cancer Database, US 1998 to 2012	Treatment trends and Long-term Survival Associated with Cryotherapy and partial nephrectomy for small renal masses in the National Cancer Database using propensity score matching	RCCs treated with CA (N=6,701) or PN (N=51,135) Overall survival outcome propensity score matched (N=6,229 in each group) and also adjusted	https://www.ncbi.nlm.nih.gov/pubmed/30808185	Kitley 2019
11	Retrospective cohort NCI SEER database, US Jan 2004 to Dec 2014	Partial nephrectomy vs cryoablation for T1a renal cell carcinoma: A comparison of survival benefit stratified by tumour size	Review of all patients in database diagnosed with RCC and treated with PN (N=17,644) or CA (N=868) Propensity score matching of 2088 patients (1044 in each group) Analysis of overall survival and cancer-specific survival outcomes adjusted	https://www.ncbi.nlm.nih.gov/pubmed/30836219	Liao 2019
12	Retrospective cohort IRCCS Ospedale San Raffaele, Italy 2000 to 2013	Minimally Invasive Partial Nephrectomy Versus Laparoscopic Cryoablation for Patients Newly Diagnosed with a Single Small Renal Mass	Patients treated with PN (N=206) or LCA (N=166) for a small renal mass (≤ 4 cm) Analyses of perioperative outcomes and renal function adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/28723359	Fossati 2015
13	Retrospective cohort Nationwide Inpatient Sample (NIS), US Oct 2008 to 2010	Utilization and perioperative complications of laparoscopic cryoablation vs. robotic partial nephrectomy for localized renal tumors	Patients with a primary diagnosis code of cancer of the kidney (ICD-9-CM 189.0) who underwent LCA (N=4,241) or PN (N=10,034) Analysis of postoperative complications adjusted for potential confounding	https://www.ncbi.nlm.nih.gov/pubmed/26200540	Weinberg 2015
14	Retrospective cohort Washington University, US Jul 2000 to Sep 2012	Renal cryoablation versus robot-assisted partial nephrectomy: Washington University long-term experience	Patients who underwent LCA (N=149), PCA (N=118) or RPN (N=233) for contrast-enhancing renal masses that were concerning for RCC on preoperative imaging Analysis of perioperative morbidity, renal function and recurrence outcomes adjusted	https://www.ncbi.nlm.nih.gov/pubmed/24283518	Tanagho 2013

#	Type of study design ¹⁶	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication
15	Retrospective cohort Medical University of Vienna, Austria 2004 to 2010	Perioperative, oncologic, and functional outcomes of laparoscopic renal cryoablation and open partial nephrectomy: a matched pair analysis	Review of patients who underwent LCA (N=41) or matched patients who underwent PN (N=82) for an incidental, solid, clinical T1aN ₀ M ₀ renal tumour Propensity score matched. Analysis of complications, renal function and recurrence-free survival	https://www.ncbi.nlm.nih.gov/pubmed/21568698	Klatte 2011
16	Prospective cohort Korea University School of Medicine, South Korea Apr 2004 to Jun 2007	A matched-cohort comparison of laparoscopic renal cryoablation using ultra-thin cryoprobes with open partial nephrectomy for the treatment of small renal cell carcinoma	Patients who underwent LCA (N=20) or PN (N=20) with pathologically confirmed RCC and tumour < 4 cm Matched on tumour characteristics and timeframe Analysis of peri- and postoperative and oncological outcomes	https://www.ncbi.nlm.nih.gov/pubmed/19688128	Ko 2008
17	Retrospective cohort New York University School of Medicine Jul 2002 to Jul 2005	A matched-cohort comparison of laparoscopic cryoablation and laparoscopic partial nephrectomy for treating renal masses	Patients with renal masses who underwent LCA (N=15) and matched patients who underwent PN (N=15 from a sample of 104) Analysis of peri- and postoperative outcomes and oncological outcomes	https://www.ncbi.nlm.nih.gov/pubmed/17092288	O'Malley 2007

Abbreviations: CA, cryoablation; eGFR, estimated glomerular filtration rate; LCA, laparoscopic cryoablation; NCI, National Cancer Institute; PCA, percutaneous cryoablation; PN, partial nephrectomy; RCC, renal cell carcinoma; RFA, radiofrequency ablation; RPN, robot-assisted partial nephrectomy; SEER, Surveillance, Epidemiology and End Results.

18. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). Please do not attach full text articles, this is just intended to be a summary.

Three yet to be published studies were identified: one RCT comparing CA with PN is due for completion in 2023, one feasibility RCT comparing PN, RFA and CA is completed but no results are available, and one RCT comparing ablation with surveillance has a protocol available but is not noted on any clinical trial registers.

	Type of study design	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)	Website link to research (if available)	Date
1.	RCT Aarhus University Hospital, Denmark	Robot-assisted Surgical Resection vs. Cryoablation of Localised Renal Cancer (ROAST)	Active, not yet recruiting Estimated enrolment: 190 Patients diagnosed with a pT1a RCC to be treated with either robotic PN or CA. Primary endpoint: loss of renal function 6 and 12 month after treatment. Secondary endpoints: recurrence free survival 1, 3 and 5 years after treatment, readmission and complication rates.	https://clinicaltrials.gov/ct2/show/NCT03390413	Primary completion date: 2023
2.	Feasibility RCT Various locations, UK	A Feasibility Study for a Multicentre Randomised Controlled Trial to Compare Surgery With Needle Ablation Techniques in People With Small Renal Masses (4cm) (CONSERVE)	Completed Actual enrolment: 17 Patients with small renal mass (< 4 cm) to be treated with PN, RFA or CA Primary outcome: Proportion who accept randomisation Secondary outcomes: QoL (various measures), anxiety/depression, difference in pre and post CT scans, effectiveness	https://clinicaltrials.gov/ct2/show/NCT01608165	Actual completion date: Jan 2015 (no published results available)

	Type of study design	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)	Website link to research (if available)	Date
3.	Feasibility RCT Various, UK	SURAB Study- A randomised study comparing Ablation with active SURveillance, in the management of incidentally diagnosed small renal tumours: a feasibility study	Unknown status – protocol only available Estimated enrolment: 60 Patients with small renal tumours to be treated with ablation (CA, RFA or MWA) or surveillance Primary outcome: recruitment and retention rates Secondary outcomes: QoL (various measures), anxiety/depression	https://nil-admin.nihr.ac.uk/document/download/2007103	NR

Abbreviations: CA, cryoablation, MWA, microwave ablation; NR, not reported; PN, partial nephrectomy; RCC, renal cell carcinoma; RCT, randomised controlled trial; RFA, radiofrequency ablation; UK, United Kingdom.

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

REDACTED

- 19. List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):**

Royal Australian and New Zealand College of Radiologists (RANZCR) - REDACTED

Interventional Radiologists of Australasia (IRSA) – REDACTED

- 20. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):**

Same as above

- 21. List the consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):**

Kidney Health Australia – REDACTED

- 22. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:**

None (but see Q11d)

- 23. Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):**

REDACTED

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

Renal cell carcinoma (RCC, kidney cancer that starts in cells that line the tubules) is the most common type of kidney cancer, accounting for about 90% of cases. Kidney cancer is the 12th most common cancer worldwide and accounts for 5% and 3% of all adult malignancies in men and women, respectively. In Australia in 2015, the age standardised incidence rate was 12.7 per 100,000 (17.5 for males and 8.2 for females) and the age-standardised mortality rate was 3.4 per 100,000 (4.8 for males and 2.2 for females). Risk in Australia increased with increasing age, being 1 in 96 up to age 75 and 1 in 65 up to age 85.¹⁷ As the world's population ages, and the prevalence of known risk factors increases, the economic and humanistic burden of kidney cancer on individuals and society is predicted to increase significantly. In Australia, the age-standardised incidence has steadily increased since 1982 from 6.2 per 100,000; however, mortality has decreased slightly from 3.9 per 100,000 since 1982.¹⁷

Apart from older age and sex, other risk factors for developing RCC include obesity, high blood pressure, and smoking. Symptoms of kidney cancer include: haematuria, anaemia, back pain, and leg/ankle oedema. People often start to have symptoms only once the tumor grows into surrounding tissues and organs and may therefore have advanced disease at diagnosis. However, due to the increased use of cross-sectional imaging, a growing number of renal tumours are incidentally discovered at earlier stages which increases chances of treatment success. Kidney cancer is stratified into four stages (I-IV). Stage I (T1) is defined as tumor size up to 7 cm in diameter, that is confined to the kidney. T1 can be further subdivided into T1a which is ≤ 4 cm and T1b which is > 4 cm to 7 cm. Small renal masses (≤ 4 cm) are the focus of this request for MBS funding of cryoablation. Five-year survival rates for T1 kidney cancer are high, with published estimates including 81% in the US,¹⁸ 90% in Canada,¹⁹ and 97% in Germany.²⁰

25. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

It is proposed that MBS-funding for cryoablation be limited to the treatment of small renal masses (i.e. T1a tumours ≤ 4 cm) in patients who are considered not suitable for the clinically superior surgical option, partial nephrectomy. Unsuitability for surgery would be considered on a patient-by-patient basis but may include one or more of the following:

- Increased age and/or frailty
- Presence of comorbidities
- Solitary kidney
- Compromised renal function
- Bilateral tumours
- Technical difficulty in performing partial nephrectomy.

¹⁷ <https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/summary>

¹⁸ American Cancer Society. What Are the Key Statistics About Kidney Cancer? available at: <https://www.cancer.org/cancer/kidney-cancer/about/key-statistics.html> 2017.

¹⁹ Canadian Cancer Society. Survival statistics for kidney cancer. available at: <http://www.cancer.ca/en/cancer-information/cancer-type/kidney/prognosis-and-survival/survival-statistics/?region=on> 2017.

²⁰ Doeahn C, Grunwald V, Steiner T, Follmann M, Rexer H, Krege S. The Diagnosis, Treatment, and Follow-up of Renal Cell Carcinoma. Dtsch 2016;113:590-6.

26. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

Following identification of a small renal mass, patients would be referred to a urologist who, in consultation with the patient, would select the most appropriate treatment option. Assessments would include the following:²¹

- Physical examination
- Laboratory examination – including creatinine, haemoglobin, erythrocyte sedimentation rate (ESR), alkaline phosphatase (ALP), lactate dehydrogenase, corrected serum calcium and estimated glomerular filtration rate (eGFR)
- Imaging – including (i) four-phase computed tomography (CT) to examine kidney mass appearance and enhancement characteristics (if renal function allows), (ii) chest x-ray ± chest CT to identify evidence of tumour spread and (iii) bone scan if elevated corrected serum calcium or ALP to identify bone metastases
- If active surveillance or ablation (cryo or radiofrequency) are being considered, a biopsy should be performed. In the case of ablative treatment, this may be performed prior to or during the procedure.

In patients undergoing active treatment (i.e. surgery or ablation) a pre-anaesthetic consult would be required.

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service:

Cryoablation is a well-established technology for the treatment of many benign and malignant tumours and lesions. Cryoablation destroys tissue by freezing the cancer cells. Very precise targeting and control of the extremely cold energy allow for efficient destruction of tumor cells while leaving healthy kidney tissue intact and functional.²²

The cryoablation procedure

To freeze the cancer, special ultra-thin probes called cryoablation needles are inserted into the site targeted for ablation. Argon gas is delivered under pressure into a small chamber inside the tip of the needle where it expands and cools, reaching a temperature well below -100° Celsius. This produces an iceball of predictable size and shape around the needle. This iceball engulfs the tumor, causing the tumour cells to expand within the iceball. At least two cycles of this process are performed to lyse the cell membrane. This ensures adequate killing of the cancerous cells as well as a small margin of surrounding tissue, while sparing healthy kidney structures. The layout of the Visual-ICE Cryoablation System is shown in Figure 1.

Cryoablation approaches

A few approaches can be used to perform renal cancer cryoablation, so the physician can customise the treatment to accommodate the patient's general health as well as the size and location of the tumor. A minimally invasive approach, rather than an open surgical approach, is usually preferred.

Percutaneous approach

The minimally invasive approach most frequently chosen is percutaneous ablation. With percutaneous access, no incisions are made. The patient is positioned in a CT (computerized tomography) or MRI (magnetic resonance imaging) scanner. The cryoablation needles and thermal sensors are inserted through the skin and positioned in the tumor under the image guidance of CT, MRI or ultrasound and the entire procedure is monitored using CT or MRI. Image-guided percutaneous cryoablation may be performed under conscious sedation, local anaesthesia, or general anaesthesia.

²¹ Rao K and Royce P.L. (2011) Incidentally detected small renal masses: investigation and management. Australian Family Physician 40(10): 776-782.

²² <https://www.galilmedical.com/treatments/kidney-cancer/>

Laparoscopic approach

Laparoscopic-guided kidney cryoablation, also a minimally invasive approach, is conducted using 3-4 small incisions through which instruments are inserted. A laparoscopic ultrasound probe is inserted through one of these incisions to send images to a screen so the physician can visualize the kidney, appropriately position the cryoablation needles, observe the iceball formation and ensure tumor destruction. Laparoscopic cryoablation is almost always performed under general anaesthesia.

Open surgery

Renal cryoablation can also be performed during traditional open surgery, although this approach is rarely used today.

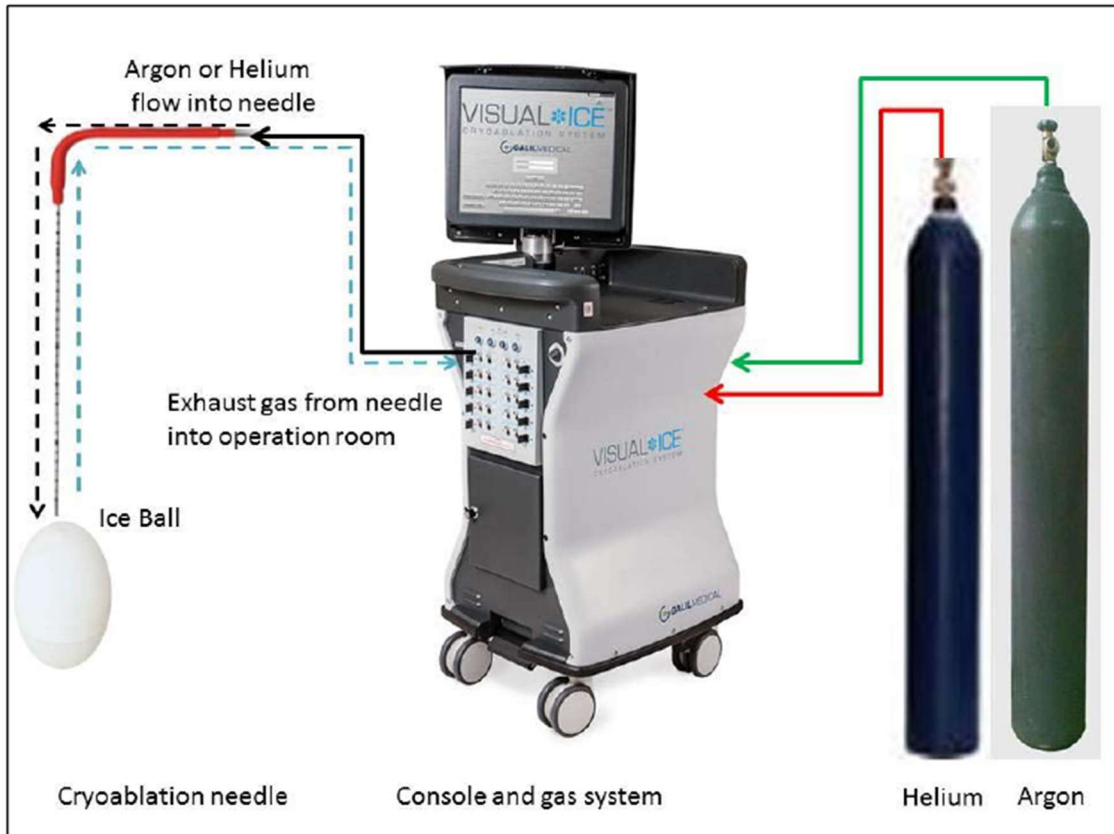


Figure 1 Principal cryoablation system layout.

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

Renal cryoablation can be carried out using any suitable cryoablation system, including the Visual-ICE Cryoablation System which is trademarked.

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

Cryoablation is an approach that is best suited to patients with small renal masses who are not considered suitable candidates for the surgical option, partial nephrectomy. While it is not a new approach, it is not currently MBS-funded.

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

The only limitation would be availability of an appropriate cryoablation system.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered at the same time as the proposed medical service:

Imaging using CT, MRI or ultrasound, dependent on the approach used. For percutaneous cryoablation, CT is the imaging modality most used.

32. If applicable, advise which health professionals will primarily deliver the proposed service:

Interventional radiologists if a percutaneous approach is used and surgeons if an open or laparoscopic approach is used. It is expected that the majority of cryoablation procedures would use the percutaneous approach, because the population of interest is those who are not considered suitable candidates for surgery (partial nephrectomy).

33. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

If performed percutaneously, cryoablation should only be delivered by an interventional radiologist.

34. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

Cryoablation should be delivered by a suitably trained interventional radiologist if performed percutaneously. Urologists are the clinicians most likely to refer patients for the procedure.

35. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

- Experienced medical proctor
- Product onboarding training program
- Trained BTG personnel to provide in-service support to system operators
- Case reviews
- Periprocedural advice and management

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select ALL relevant settings):

- Inpatient private hospital (admitted patient)
- Inpatient public hospital (admitted patient)
- Private outpatient clinic
- Public outpatient clinic
- Emergency Department
- Private consulting rooms - GP
- Private consulting rooms – specialist
- Private consulting rooms – other health practitioner (nurse or allied health)
- Private day surgery clinic (admitted patient)
- Private day surgery clinic (non-admitted patient)
- Public day surgery clinic (admitted patient)
- Public day surgery clinic (non-admitted patient)
- Residential aged care facility
- Patient's home
- Laboratory
- Other – please specify below

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

The procedure could be carried out in a public or private setting. The majority of procedures currently being undertaken in Australia take between 1 to 2 hours, are well tolerated, and the patient is discharged home on the same day.

37. Is the proposed medical service intended to be entirely rendered in Australia?

- Yes
- No – please specify below

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

There are two main comparators to cryoablation in the population of patients who are not deemed suitable for surgery: active surveillance/deferred therapy and radiofrequency ablation (RFA)

Partial nephrectomy will be included as a supplementary comparator because some patients may prefer to use a less invasive treatment option than surgery, even though it is known to be clinically inferior.

39. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

Yes – partial nephrectomy

MBS Item 36522 – NEPHRECTOMY, partial

MBS Item 36525 – NEPHRECTOMY, partial, complicated by previous surgery on the same kidney

No – RFA (no item numbers specifically for small renal mass/renal cancer indication) and active surveillance/deferred treatment.

40. Define and summarise the current clinical management pathway/s that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards, including health care resources):

Follow up visits and CT examinations in the first 12 months post intervention for each treatment type are shown below. Most often, patients are followed up within 3 months of cryoablation, with follow-up multiphase CT or MRI scan.

Table 6 Follow-up schedule for the intervention and comparator procedure

	3 months	6 months	9 months	12 months
<i>Cryoablation</i>	✓	✓		✓
<i>Active surveillance</i>	✓	✓	✓	✓
<i>Radiofrequency ablation</i>	✓	✓		✓
<i>Partial nephrectomy</i>		✓		✓

41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

In addition to (i.e. it is an add-on service)

Instead of (i.e. it is a replacement or alternative)

(b) If instead of (i.e. alternative service), please outline the extent to which the current service/comparator is expected to be substituted:

The expected substitution rates shown below are estimates only. A more detailed exploration of the expected substitution of each of the comparators will be conducted for the submission:

- Active surveillance – 20% (it is expected that if cryotherapy was more readily available and affordable, some patients currently managed using active surveillance may choose to undergo intervention instead)
- Radiofrequency ablation – 50% (it is expected that if cryotherapy was more readily available and affordable, some patients currently managed using radiofrequency ablation may choose to undergo cryoablation instead)
- Partial nephrectomy – 10% (it is expected that some patients may elect to have a less invasive procedure that is readily available and affordable, even though it is known to be less effective)

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service, including variation in health care resources (Refer to Question 39 as baseline):

It is expected there will be very little change from the current clinical management pathway, as shown in Attachment B. As outlined in Question 41(b) the only changes will be an increase in the number of cryoablation services performed due to its greater availability and affordability, a substantial decrease in the number of radiofrequency ablation procedures, and slight decreases in the number of partial nephrectomies and number of patients undergoing active surveillance.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

Examination of the considerable amount of clinical data available is currently underway but at this stage it is expected that the following claims will be made for cryoablation:

- versus active surveillance/delayed therapy – superior in terms of efficacy and inferior in terms of safety
- versus radiofrequency ablation – non-inferior in terms of efficacy and safety
- versus partial nephrectomy – inferior in terms of efficacy and superior in terms of safety

44. Please advise if the overall clinical claim is for:

As noted above, examination of the considerable amount of clinical data available is currently underway but at this stage it is expected that the following overall clinical claim will be made for cryoablation:

- Superiority
 Non-inferiority

45. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes:

Primary

Major treatment-related complications (e.g. death, haemorrhage, renal injury, renal dialysis, ureteric injury, renal vessel injury, renal pelvis injury, small bowel injury, injury to other adjacent structures, pneumonia, fistula, renal failure or serious infection)

Development/worsening of CKD

Change in EGFR

Secondary

Minor treatment-related complications (e.g. probe site pain, bleeding not requiring transfusion, transient urinary leakage or minor infection)

Clinical Effectiveness Outcomes:

Primary

Overall survival or mortality rate

Disease-specific survival

Secondary

Disease-free survival

Local recurrence

Progression-free survival

Quality of life

Length of hospital stay

Operative time

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population:

REDACTED

47. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

REDACTED

48. How many years would the proposed medical service(s) be required for the patient?

REDACTED

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

REDACTED

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

REDACTED

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The following resource use is likely to feed into the overall cost of cryotherapy:

- Cryotherapy equipment – i.e. cost of Cryotherapy System and Procedure Packs
- Interventional radiologist, time (percutaneous procedures – expected to be the vast majority of procedures)
- Surgeon, time (open or laparoscopic procedures)
- Radiology suite or operating theatre usage
- Radiographer time (for machine operation and coordination with nursing staff)
- Other consumables (e.g. dressings)
- Anaesthetist, time
- Anaesthetic
- Follow-up imaging
- Dedicated nursing staff for post intervention care
- Overnight stay in hospital (if required).

A detailed examination of these costs will be provided in the submission to MSAC.

52. Specify how long the proposed medical service typically takes to perform:

Cryoablation typically takes 1-2 hours to perform.

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

The proposed MBS item descriptor is presented below. This is based on the existing descriptors for RFA and MWA in patients with primary malignant tumour of the liver (Items 50950 and 50952).

The proposed descriptor may be refined depending on the outcome of discussions with the Department, feedback from PASC, and the availability of clinical evidence.

Category 3 – THERAPEUTIC PROCEDURES
SUSPECTED PRIMARY MALIGNANT TUMOUR OF THE KIDNEY (≤ 4 CM), destruction of, by percutaneous, laparoscopic or open cryoablation (including any associated imaging services), where partial nephrectomy is not considered suitable or feasible Fee: \$817.10*

* This is the same as the fee for percutaneous RFA or MWA (Item 50950) and laparoscopic or open RFA or MWA (Item 50952) for the treatment of unresectable primary malignant tumour of the liver.