NICE advice

Arctic Sun 5000 for therapeutic hypothermia after cardiac arrest

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Arctic Sun 5000. It is used for therapeutic body temperature management.
- The **innovative aspects** are that it is less invasive than endovascular systems and is designed to cool more efficiently than conventional external methods because of the adhesive, repositionable gel pads it uses. It works by adjusting the water temperature in the gel pads every 2 minutes in response to the patient's body temperature, which is constantly monitored using a probe.
- The **intended place in therapy** would be instead of standard surface cooling systems to induce mild hypothermia in people who are comatose after having a cardiac arrest in or out of hospital, and for subsequent rewarming.

- The **main points from the evidence** summarised in this briefing are from 4 studies (2 randomised controlled trials and 2 comparative observational studies), including a total of 362 adults. Arctic Sun 5000 appears to achieve therapeutic cooling faster than standard cooling blankets and takes about the same time as endovascular cooling systems. In the randomised study comparing it with endovascular cooling, people in the Arctic Sun 5000 group had significantly fewer complications (bleeding and sepsis). But there was no significant difference in adverse effects in the randomised study comparing Arctic Sun with surface cooling. No studies showed a statistically significant difference in clinical outcomes between Arctic Sun 5000 and either surface or endovascular cooling methods.
- **Key uncertainties** around the evidence are the lack of studies showing a difference in clinical outcomes between Arctic Sun 5000 and other cooling methods.
- The **cost** of Arctic Sun 5000 is £20,600 (exclusive of VAT), with a cost per patient of between £696.69 and £833.17 per treatment. The **resource impact** is uncertain. Arctic Sun 5000 would represent an increased cost compared with conventional cooling blankets, but this may be offset if less staff time is needed to operate it, or if it resulted in fewer complications. Arctic Sun 5000 may cost less than endovascular cooling systems while offering similarly effective cooling, and may have a reduced risk of complications.

The technology

The Arctic Sun 5000 temperature management system (Medivance/Bard) is a non-invasive system for controlling and monitoring body temperature within the range of 32°C to 38.5°C. It is intended for use in adults who are comatose after sudden cardiac arrest in or out of hospital, with the aim of inducing mild hypothermia to reduce brain injury and improve neurological outcomes. Mild hypothermia (32°C to 36°C, as recommended by European Resuscitation Council and European Society of Intensive Care Medicine guidelines) is induced as soon as possible after a cardiac arrest. The specific target temperature can be set by the lead clinician or according to hospital guidelines.

Arctic Sun 5000 has 3 modes: cooling, rewarming and maintaining temperature within the healthy range of 36°C to 37°C (normothermia).

Arctic Sun 5000 comprises 2 main components:

- A closed loop system, which consists of a control module with a touch screen, water reservoir and water heater.
- Four disposable, single-use, repositionable adhesive gel pads (2 for the upper body and 2 for the thighs). Temperature-controlled water is circulated through channels in the gel pads.

The gel pads are available in 4 sizes. The correct size is chosen for each patient to ensure that 40% of the body surface is covered, which is needed for efficient temperature control. The gel pads are MRI, CT and X-ray compatible. Their inner layer is made of a heat conductive hydrogel that sticks to the skin. The middle layer includes channels through which the water is circulated, and the outer layer is designed to insulate the circulating water and maintain its temperature.

Arctic Sun 5000 must be used with an indwelling Yellow Springs Instrument 400 series temperature probe. The probe is inserted into a core site, such as the bladder, rectum or oesophagus, and then connected to the control module so that core temperature can be monitored continually. A second temperature probe can be added at a core site in order to confirm the reading if needed. The gel pads are applied to the patient then connected to the control module, and water is circulated through the pads to prime the lines. Once primed, the water temperature can be set using the control module.

The operator sets the target body temperature, which can be saved into the system for future use. The control module automatically adjusts the temperature of the water in the gel pads every 2 minutes to maintain target core body temperature. Target temperature is maintained for 24 hours, after which the system can be used to rewarm the patient.

In addition to therapeutic cooling, patients should have standard critical care measures including intravenous sedation and muscle relaxants to prevent shivering. Controlled rewarming by any method is usually done over a number of hours at a rate of 0.25°C to 0.5°C per hour (as recommended by European Resuscitation Council and European Society of Intensive Care Medicine guidelines).

Arctic Sun 5000 is the current version of the device; the previous version, Arctic Sun 2000, was discontinued in 2016. The 2 versions are functionally identical and differ only in the user interface; Arctic Sun 5000 has a touchscreen which displays a patient trend indicator and status graph.

Innovations

The gel pads are designed to provide rapid cooling. The closed loop system of temperature monitoring and automatic adjustment is intended to reduce the amount of time needed for nurses to measure core temperature and manually adjust the temperature regulation system. Arctic Sun 5000 is also designed to be less invasive than endovascular systems.

Current NHS pathway or current care pathway

NICE interventional procedures guidance on therapeutic hypothermia following cardiac arrest states that the evidence on safety and efficacy is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, audit and consent. The guidance notes that after a cardiac arrest, comatose patients who have a return of spontaneous circulation can be cooled to a core temperature of between 32°C and 34°C with the aim of reducing brain injury and improving neurological outcome. This is in accordance with the European Resuscitation Council and European Society of Intensive Care Medicine guidelines, although these guidelines also state that milder therapeutic temperatures up to 36°C may be beneficial for some patients.

In current standard care, mild hypothermia is induced by using either surface techniques, such as heat-exchange cooling pads, or invasive techniques, including endovascular cooling devices.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function to Arctic Sun 5000:

- Blanketrol (CSZ Medical)
- Flex.Pad (EMCOOLS)
- CritiCool (MTRE)
- Thermogard XP (Zoll); NICE has produced a medtech innovation briefing on this technology
- RhinoChill (Benechill); NICE has produced a medtech innovation briefing on this technology.

Population, setting and intended user

Artic Sun 5000 is most likely to be used for the induction, maintenance and re-warming phases of therapeutic hypothermia in a critical care setting by any critical care staff. It is designed for use in adults who are comatose after a sudden cardiac arrest in or out of hospital, and who have a return of spontaneous circulation. The system would replace current standard cooling methods with little expected change to the current care pathway.

Costs

Table 1 Device costs

Component	Cost	Additional information
Arctic Sun 5000	£20,600.00	Multiple use
Temperature in cable	£116.36	
Temperature out cable	£93.09	
Fill tube	£37.23	
Fluid delivery line	£1,394.41	
Shunt line	£13.96	Single use (optional)
Drain bag	£26.71	
Drain tube	£32.58	Multiple use
Foley catheter temperature sensor	£349.10	Multiple use: 14, 16 or 18 Fr
Arctic gel pad kit	£628.30	Single use for duration of treatment: extra small, medium or large
Arctic gel pad: universal kit (4 universal pads packaged individually, 1 used per patient)	£545.90	Single use for duration of treatment. Universal pads are intended to be used in addition to standard gel pad kits, to ensure 40% body coverage of larger people
Primary (Foley) temperature probe	£10.30	Single use

Secondary temperature probe	£1.59	Single use, optional
Oesophageal/rectal probe 9 Fr	£139.64	
Maintenance		
Option 1 (labour and parts)	£2,800.00	Per year
Option 2 (labour only)	£1,900.00	

Assuming an 8-year lifespan for the device, used at a rate of 100 patients per year (800 uses in total), the cost per treatment ranges from £697 to £833.

The cost per treatment for single-use components only is £556 to £738.

Costs of standard care

Tables 2 and 3 show example costs for surface and endovascular cooling systems.

Table 2 Cost of surface cooling (Blanketrol III)

Component	Cost	Additional information
Cooling control unit	£9,495.00	Multiple use
CSZ reusable connecting hose (2.7 m)	£79.00	
CSZ patient temperature probe cable	£40.00	
CSZ MaxiTherm Lite patient vest	£133.90	Instead of MaxiTherm Lite adult (below), single use
CSZ MaxiTherm Lite adult	£129.00	Instead of patient vest (above), single use
CSZ Kool Kit	£315.60	Single use
CSZ Kool Kit (large)	£347.12	

Depending on which kit is used, the price per patient per treatment for single-use components only ranges from £129 to £347.

Table 3 Cost of endovascular cooling (Thermogard XP)

Component	Cost	Additional information
Heat exchanger unit	£21,500.00	Multiple use
Temperature probe interface cable	£89.00	
Propylene glycol coolant (1 gallon)	£30.00	
Coolant well lid	£150.00	
Intravascular catheters	Cool Line: £318.27 Icy: £509.85 Quattro: £637.94	Single use, only 1 needed
Start-up kit (model CG-500D)	£235.87	Single use
Foley temperature probe	£10.00	
Hospital monitor interface accessory	£1,759.00	Optional
Secondary temperature probe	£1.54	This would need to be supplied by the hospital
All costs are taken from the NICE medtech innovation briefing on Thermogard XP.		

Depending on which catheter is used, the cost per patient treatment for single-use components only ranges from £574 to £894 (excluding VAT).

Resource consequences

Arctic Sun 5000 would add additional costs compared with other surface cooling methods, but these may be offset if it resulted in reduced staffing costs or if it reduced the cost of

treating neurological damage by improving clinical endpoints. Compared with endovascular temperature management systems such as Thermogard XP, Arctic Sun 5000 could reduce costs depending on the consumables used and lifespan of the systems involved. The resource consequences of using Arctic Sun 5000 may also depend on whether it reduces the risk of complications compared with endovascular cooling, although this benefit may also apply to other non-invasive cooling methods.

The company provides training as part of the purchase cost. This includes 2 self-learning modules and a hands-on 3-hour workshop tailored to each hospital's needs. Clinical specialists are available to provide ongoing training and support. Advanced training is offered to selected members of the clinical team so that they can provide independent in-house training and support.

Arctic Sun systems are currently used in 30 NHS hospitals.

Regulatory information

The console of the Arctic Sun system was CE marked as a class IIb device, and the gel pads as a class I device, in May 2004. Bard distributes the device in the UK.

A search of the Medicines and Healthcare products Regulatory Agency website revealed 2 field safety notices for this technology.

- FA2015-30: premature drainage of the internal control panel coin cell battery responsible for maintaining the system clock and static RAM. This could render the device unresponsive upon system start-up. Bard inspected all units shipped from April 2011 to February 2015 to determine if they were affected by this issue, and affected parts were replaced by a Bard technician. The company has confirmed that this issue has now been resolved.
- FA2016-47: Bard completed an internal health hazard evaluation and concluded that there is a highly remote probability of risk of harm to a patient or user being exposed to nontuberculous mycobacterium through the Arctic Sun system based on use of the device under existing labelling. A field safety notice was handed to all personnel using the device.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No equalities considerations were identified with the use of Arctic Sun 5000.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

This briefing summarises 4 studies including a total of 362 patients: 2 randomised controlled trials (n=144) and 2 comparative observational studies (n=218). One of the randomised controlled trials and 1 observational study compared Arctic Sun with an endovascular cooling system, Coolgard (Zoll). The other studies compared Arctic Sun with cooling blankets.

Table 4 summarises the clinical evidence including its strengths and limitations.

Overall assessment of the evidence

The studies which comprise the evidence base use robust designs. Two of these studies are underpowered to detect their clinical outcomes, but this is to be expected in a high-risk patient population. Two of the studies compare Arctic Sun 5000 with named

comparators used in standard care. None of the studies indicated that Arctic Sun 5000 provides better clinical outcomes than either cooling blankets or endovascular cooling systems.

The studies were not done in the UK, which may limit their generalisability, but all outcomes reported are relevant to the NHS care pathway.

Arctic Sun 5000 is used in a particularly high-risk patient group, so serious adverse events should be expected to occur more frequently. In light of this, the complications data in table 4 only include device-related or hypothermia-related complications.

Table 4 Published evidence

Pittl et al. (2013)	
Study size, design and location	80 patients. Germany, single centre. Prospective, randomised (1:1) study on patients who survived in-hospital and out-of-hospital cardiac arrest.
Intervention and comparator	Intervention: Arctic Sun (n=40). Comparator: Coolgard endovascular system (Zoll) (n=40). All patients were cooled at 33°C core body temperature for 24 hours followed by active rewarming. Patients were followed-up for 72 hours.
Key outcomes	Neuro-specific enolase levels at 72 hours did not differ significantly between groups. Overall survival was not significantly different between groups. Survival with good neurological outcome (CPC 1–2) during hospitalisation was identical in both groups (35.9%). There was no significant difference in cooling rate between the 2 devices. Stability at the target temperature was significantly better in the Coolgard group. Significantly more Coolgard patients had bleeding complications compared with Arctic Sun patients.

Strengths and limitations	The study used 1:1 randomised methods but was not double blinded or adequately powered to detect differences in clinical outcomes. Some time recordings may not be reliable because they were based on witness or paramedic testimony reporting the patients' time of collapse from cardiac arrest.
Heard et al. (2010)	
Study size, design and location	64 patients. US, 6 university-affiliated hospitals. Multicentre randomised (1:1) trial of haemodynamically stable comatose survivors of out-of-hospital cardiac arrest.
Intervention and comparator	Intervention: Arctic Sun (n=34). Comparator: standard post-resuscitative care inducing hypothermia using cooling blankets and ice (n=30).
Key outcomes	The proportion of subjects cooled below the 34°C target at 4 hours was not significantly different between groups. The median time to target temperature was significantly faster in the Arctic Sun group. At 3 months follow-up, overall survival was not significantly different between the 2 groups. Survival with good neurological outcomes (CPC 1–2) was also not significantly different between groups. Rates of adverse events were not significantly different between groups. The rate of overshooting (cooling to below 32°C) during induction was significantly higher in the standard cooling group.
Strengths and limitations	The study used 1:1 randomisation methods used at each centre but was not double blinded. Most centres were inexperienced in therapeutic hypothermia, and some centres had a gap of several months between recruitments. There was no standardised protocol for pharmaceutical paralytics, which varied between centres. The study was also supported by company grant.
Tomte et al. (2011)	

Study size, design and location	167 patients. Norway, single centre. Comparative 2-armed observational study enrolling consecutive comatose patients after out-of-hospital cardiac arrest treated with mild therapeutic hypothermia.
Intervention and comparator	Intervention: Arctic Sun (n=92). Comparator: Coolgard (n=75).
Key outcomes	There were no significant differences in survival to final hospital discharge with good neurologic function (CPC 1–2) between groups. Lengths of intensive care unit stay and respirator dependency, rates of mild therapeutic hypothermia discontinuation, and post-cooling fever were not significantly different between the 2 groups. There was no significant difference in time to achieve target temperature (34°C) between the 2 groups. Infection rates and antibiotic treatment, arrhythmias, level of haemodynamic support, transfusion rates, presence of seizures or shivering, use of paralytic agents, and need for dialysis were also comparable between the 2 groups.
Strengths and limitations	Consecutive patient enrolment may have minimised patient selection bias. All out-of-hospital cardiac arrest patients in the study period were included, creating a large patient cohort. The study was not randomised or blinded, and the hospital initially used Coolgard before Arctic Sun was introduced, which may have introduced bias in terms of clinical developments in hospital standard care. The study was underpowered to assess neurologic-intact survival as an outcome between the 2 groups.
Shinada et al. (2014)	
Study size, design and location	51 patients. Japan, single centre. Consecutive enrolment of patients who did not regain consciousness after return of spontaneous circulation following cardiogenic cardiac arrest.

Intervention and comparator	Intervention: Arctic Sun 2000 (n=40). Comparator: conventional standard cooling blankets (n=11).
Key outcomes	Time to achieve the target temperature was significantly shorter with Arctic Sun than with standard cooling blankets. There was no significant difference between groups in number of patients achieving CPC 1–2 at 30 days' hospitalisation. There were no differences in the incidence of complications during hypothermia, including pneumonia and bleeding, between the 2 groups. Minimal body temperature achieved during therapeutic hypothermia was significantly lower in the standard cooling group.
Strengths and limitations	Consecutive patient enrolment may minimise patient selection bias and all patients meeting inclusion criteria in the study period were included. However, the study was non-randomised, retrospective and unblinded. There were also more patients in the Arctic Sun arm than the much smaller comparator arm.

Recent and ongoing studies

The following relevant ongoing studies were found on ClinicalTrials.gov:

- NCT02889744 – Comparison of Cerebral SctO2 between 36°C and 33°C of Targeted Temperature Management after Cardiac Arrest. Currently recruiting, estimated completion date: September 2018.
- NCT02578823 – Targeted Temperature Management After In-Hospital Cardiac Arrest. Currently recruiting, estimated completion date: April 2018.
- NCT00827957 – Comparing Therapeutic Hypothermia Using External and Internal Cooling for Post-Cardiac Arrest Patients. Study completed.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 3 specialist commentators said that they were currently using the device at varying intervals. One had used the Arctic Sun 5000 as part of the Eurotherm3235 trial.

Level of innovation

The specialist commentators agreed that this device was moderately innovative, because it is a variation on standard water-cooling blankets that offers better functionality, ease of use and control.

Potential patient impact

The specialist commentators agreed that Arctic Sun 5000 is beneficial in reducing secondary neurological brain injury, meaning reduced risk of disability after recovery, less critical care and rehabilitation time, and better functional status. This includes both patients having in-hospital and out-of-hospital cardiac arrests. One specialist observed that the correct 'dose' of cooling is still not known.

Potential system impact

One specialist remarked that although Arctic Sun 5000 and its related consumables are costly, the device is very effective at managing core body temperature.

All the specialist commentators agreed that no changes to facilities or infrastructure would be needed to implement Arctic Sun 5000, but that some specialist staff training was needed. One commentator noted that cooling with the device can be nurse-led, reducing the lead-time associated with inserting catheters for endovascular cooling systems.

Two commentators felt that Arctic Sun 5000 could save costs; one thought that savings may be achieved through shortened length of stay in intensive care. Another felt that more research was needed to confirm any cost savings. One specialist said that cost savings would be achieved through a reduction in long-term costs of managing neurological injuries.

General comments

One specialist commentator reflected that although they have been using the

Arctic Sun system for a number of years, they now use it less often for warming patients. Instead, their unit chooses to keep patients at a constant temperature of 36°C by monitoring the core temperature and adding or removing standard blankets as needed. The expert noted that more of their patients needed the use of the Arctic Sun for warming than for cooling.

Specialist commentators

The following clinicians contributed to this briefing:

- Prof. Peter Andrews, consultant in anaesthetics and critical care, NHS Lothian. Honorary professor, University of Edinburgh. Prof. Andrews has been paid (travel and subsistence) by Bard to lecture on therapeutic hypothermia.
- Dr Melinda Brazier, consultant anaesthetist and intensivist, Ashford and St. Peter's Hospitals NHS Foundation Trust. No conflicts declared.
- Mrs Sharon Clitheroe, matron, Cardiac ITU, Blackpool Teaching Hospitals NHS Foundation Trust. No conflicts declared.

Development of this briefing

This briefing was developed for NICE by Cedar. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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