FAQ US Territories
EMCOOLS Flex.Pad N/Flex.Pad N Small

Indication and field of application

1. Background

Mild therapeutic hypothermia basically improves the outcome in patients with global cerebral ischemia after cardiac arrest.

Beside this therapeutic hypothermia seems to be a promising treatment as well in other types of acute hypoxic-ischemic or in brain swelling associated cerebrovascular diseases. In this context the narrow time–frame is a major issue as "time is brain". For immediate cooling without delay, methods which are easy to use, mobile and effective, are needed.

2. What is the purpose of EMCOOLS Flex.Pad N?

The indications for use of EMCOOLS Flex.Pad N is for temperature reduction in adult patients where clinically indicated, e.g. in hyperthermic patients.

The product is easy to use and provides effective cooling without any delay. Within 60 - 90 minutes from start, the patient's brain temperature will typically be lowered by 1.0°C / 1.8°F.

The core body temperature does not drop below shivering threshold (35.5 to 35.0°C / 95.9 to 95.0°F) and is tolerated by awake and non-sedated patients, who represent the majority of acute stroke patients. The safety, tolerability and efficacy of local surface cooling with EMCOOLS Flex.Pad N in awake patients was evaluated in a clinical pilot study in 10 healthy volunteers by Kallmünzer et al. in 2012.[1]

For therapeutic hypothermia the treatment has to be typically continued with other systems (e.g. with EMCOOLS Flex.Pad).

3. Neuro-protective benefits of mild therapeutic hypothermia?

Mild therapeutic hypothermia is a medical treatment to lower a patient's body temperature to 32°C–34°C / 89.6°F – 93.2°F in order to reduce neurological damages, following a period of whole-body or local insufficient blood flow (ischemia) [2].

Ischemic injury and the subsequent reperfusion injury after restoration of blood circulation are interrelated processes at the cellular level. A complex cascade of processes is starting minutes to hours after injury and continuing for up to 72 hours or longer (early excitotoxic reactions => intermediate inflammatory reactions => late apoptotic cell death).

These processes lead to progressive cell destruction, neuronal apoptosis, multi-organ dysfunction and death. The pathophysiologic mechanisms which are involved in hypothermia are incompletely understood but have been studied in cellular, animal, and human models. Many of these deleterious processes are temperature sensitive, i.e. increased by fever and attenuated or ameliorated by mild hypothermia.

4. Why do we need to cool patients immediately after symptom onset?

As already stated ischemia has a key role in various forms of brain injuries. The neurological outcome is mainly determined by the mechanisms which take place during the post-injury-period. Therefore the prevention/reduction of ischemic injuries is essential for all neuro-protective strategies. The main possibility for cell protection and to buy time for further diagnosis is to cool patients immediately after symptom onset (e.g. in potential stroke).

5. Why do we need to cool patients with acute ischemic stroke?

Currently therapeutic hypothermia is one of the most promising therapies for patients with acute ischemic stroke.

CLINICAL EVIDENCE
Growing evidence in animal and human studies has documented or suggested the beneficial outcome effects of mild hypothermia (33-36°C / 91.4-96.8°F) for ischemic stroke.

In a systematic review of animal studies (101 publications, including data from a total of 3353 animals[3]), the benefit of therapeutic hypothermia was

inversely related to the temperature achieved. Therapeutic Hypothermia (34°C/93.2°F) reduced the infarct size by more than 40%. With cooling to 35°C/95.0°F the infarct size was still reduced by 30%.

These results may support the suggestion that even very modest cooling at conditions that might be achievable for large numbers of stroke patients, could have considerable neuro-protective potential.

So far, the use of therapeutic hypothermia has been investigated in seven small feasibility studies with 145 stroke patients. Therapeutic Hypothermia was noted to be feasible with limited and well controllable side-effects, although the incidence of non-fatal pneumonia was high in one study. All investigators reported significant decreases in brain oedema and improved outcome compared with historical controls (mortality 38% *versus* 80% in the largest study[4]). Moreover, many deaths occurred during rewarming with rebound increases in ICP. A subsequent study[5] showed that ICP increases were preventable with slow and controlled rewarming.

However, none of these studies were properly controlled, and all had extended time intervals between symptom onset of stroke and initiation of hypothermia (average 22 hours in the largest study with an additional 6.5 hours before achieving target temperature). After that period of time it is very likely that much of the injury has become permanent.

TIME IS BRAIN

Stroke occurs due to an interruption in cerebral blood supply affecting neuronal function. The extended period of ischemia causes irreversible brain cell destruction (necrosis) in a non- perfused central area. The necrotic area is surrounded by a so-called penumbra zone, which is hypo-perfused but not (yet) irreversibly damaged.

As long as penumbra zone has not yet become necrotic it could be protected and rescued by immediate cooling. The salvageable zone could be increased if local blood circulation (reperfusion) starts again (e.g. after administration of clot-dissolving drugs). Typically within the first two hours after symptom onset no reperfusion takes place. This is the time frame in which therapeutic hypothermia is ideally started for the reduction of negative effects of the entire ischemic cascade.

50 % OF ALL STROKE PATIENTS HAVE FEVER

Fever (core body temperature above 38.0°C/100.4°F) is an independent negative predictor of mortality and morbidity of patients with acute neurological injury or diseases such as stroke.[6]

In the lesioned brain fever leads to:

- Swelling of cells due to water and electrolytes
- Cell death and release of cell content
- Inflammatory reactions

50% of all stroke patients have fever, due to the progressive cell destruction and subsequent inflammation processes. Fever worsens the neurological outcome, as body temperature has a strong influence on the very early steps of stroke physiopathology (i.e. within the very first hours of symptoms onset). Therefore the cooling therapy might be more effective the sooner it is started after symptom onset.

Nevertheless the restricted time window is a significant barrier, which takes advantage of these effects in a regular clinical setting. Therefore, cooling should be ideally induced within "the first golden hour" by the ambulance service team at the scene.

TEMPERATURE MANAGEMENT IN AWAKE PATIENTS

The typical emergency department patient with acute stroke is awake and not intubated.

Although two small case series[7,8] have suggested that induction of mild hypothermia in awake, non-ventilated patients could be feasible, close monitoring and aggressive patient management remain essential to obtain good outcome.

6. How can we start cooling with EMCOOLS Flex.Pad N immediately after symptom onset?

EMCOOLS Flex.Pad N appears safe and tolerable in awake volunteers.[9] Its portable design allows for the cooling therapy to be started immediately in the pre- and in-hospital setting. It takes only 1 minute to apply EMCOOLS Flex.Pad N to the patient's body surface. The system is radiolucent, MRI compatible and safe and allows for the cooling therapy to be started in the pre-hospital setting, and continued through to intensive care.

7. Are there any contraindications for using EMCOOLS Flex.Pad N?

There are no known contraindications for the use of EMCOOLS Flex.Pad N.

EMCOOLS Flex.Pad N must not be used in case of skin diseases, inflammation, burns or skin injuries. Reversible, temporary skin reactions may occur in very rare cases i.e. patients with hypersensitive skin. For further information please refer to the Instructions for Use.

Temperature reduction to > 35.0°C/95.0°F does not cause any side-effects on other medical treatments, such as thrombolysis, medication etc.[10]

Product description and performance

8. What is EMCOOLS Flex.Pad N?

EMCOOLS Flex.Pad N is based on the HypoCarbon® technology, which is a patented cooling technology that generates an immediate heat absorption from the patient's body. In doing so, HypoCarbon® withdraws the heat from the body immediately after initial contact with the patient's skin.

9. Is there a hazard to the user, patient or any third party if individual components of EMCOOLS Flex.Pad N leak?

HypoCarbon® is non-toxic and does not constitute any safety hazard or danger to the environment. There is no risk to the user, patient or third parties if it is released due to a mechanical damage. In case of leakage the substance can be easily cleaned with soapy water.

10. Do individual product components of Flex.Pad N represent a hazard to the user, patient or any third party?

All EMCOOLS products (incl. product packaging) with direct contact to the patient are latex and PVC free. Furthermore we can certify that all EMCOOLS products and product packaging are phthalates-free which means that they do not contain any hazardous plasticizers such as DEHP, DBP, BBP and DIBP. As a result EMCOOLS products represent no danger and no risk to the user, patient, third parties or the environment.

11. Does the adhesive on the back of the Flex.Pad N cause skin irritation or skin injury?

The back of the Flex.Pad N consists of a medical adhesive film which is suitable for medical products with direct skin contact such as operating sheets and bandages. The adhesive film is skin-friendly and dermatologically tested to be suitable for medical products.

The medical adhesive film guarantees optimum skin contact during application and use. At the same time it has been designed to show little resistance during removal. This ensures a skin-friendly, soft and easy removal of Flex.Pad N after use.

In patients with hypersensitive skin reversible reddening of the skin (hyperaemia) may occur in some rare cases after removing the EMCOOLS Flex.Pad N. The skin reddening is temporary and reversible (up to 24 hours after the cooling therapy) and does not cause permanent skin injury. The medical adhesive film itself does not create reddening of the skin. Permanent skin injury has not been observed in any case when compliance with the instructions for use is assured.

12. What is the ideal temperature for storing EMCOOLS Flex.Pad N?

Before use, EMCOOLS Flex.Pad N must be cooled and stored in a freezer at –8°C to –11°C / 12.2°F to 17.6°F, in order to maintain operational readiness.

13. How do I know if Flex.Pad Ns are ready to use?

The color indicator on the product packaging indicates if the Flex.Pad Ns are ready for use and have been stored at the correct temperature.
At room temperature (when unchilled) the color indicator displayed on the product packaging is **GRAY**. When precooled at correct temperature the color indicator displayed on the product packaging turns **BLUE** and Flex.Pad Ns are ready to use. If the indicator displayed on the product packaging turns **BLACK** the Flex.Pad Ns have been stored at a temperature much colder than needed and are not ready for use. In such case please check and adjust the freezer temperature according to the instructions for use (-8°C to -11°C/12.2 to 17.6°F).

14. How can I ensure that Flex.Pad N is at correct temperature and ready for use in the pre-hospital setting?

For pre-hospital applications, Flex.Pad N can be stored in one of the suitable mobile cooling units: the EMCOOLS Box for emergency vehicles or the products of the EMCOOLS Six.Pack Family which are suitable for both air rescue and ambulance cars. Both mobile cooling units can keep Flex.Pad Ns at correct temperature and ready for use over a period of 12 to 24 hours without any external power supply.

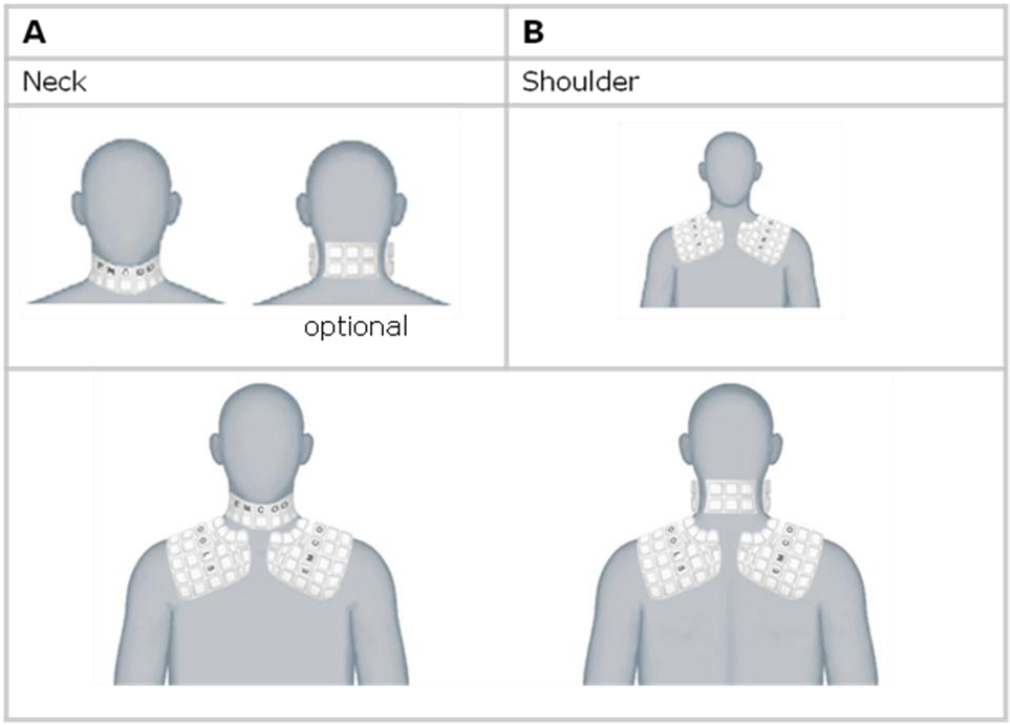
Cooling therapy

15. How many EMCOOLS Flex.Pad Ns do I need per patient?

For one patient one Flex.Pad N is needed. It consists of two pads for the shoulders, one pad for the neck and one optional pad (Flex.Pad N Small does not contain this optional pad), which can be used if needed (depending on the size of a patients neck – see image under point 16)

16. Where do I apply EMCOOLS Flex.Pad N?

EMCOOLS Flex.Pad N is applied on dry skin on shoulders and neck (see image below).



For an optimized application the cooling elements for the neck should be applied first. Depending on the size of the patient's neck the small pad for the neck can be used. In a second step the cooling elements for the shoulders should be applied as close as possible to the cooling elements of the neck. Press down all pads carefully for 3-5 seconds to allow for the adhesive film to fully adhere.

17. Can I use EMCOOLS Flex.Pad N during MRI/CT and X-Ray?

Yes, EMCOOLS Flex.Pad Ns are radiolucent, MRI compatible and safe and can be used during CT, MRI and X-Ray.

18. How do I measure the patient's temperature during the treatment?

EMCOOLS Flex.Pad N can be used with all commercially available medical monitoring systems and all medical temperature probes. However EMCOOLS recommends tympanic temperature measurement as it closely correlates with brain temperature.

19. Do patients shiver when treated with Flex.Pad N?

Patients do not shiver during treatment with EMCOOLS Flex.Pad N as core body temperature does not drop below 35.0 to 35.5°C / 95.0 to 95.9°F (shivering threshold).

20. Can I re-use Flex.Pad N?

EMCOOLS Flex.Pad N is a disposable product. It is non-sterile and designed for single use only. For hygienic reasons, disposal is required after application. EMCOOLS Flex.Pad N must be disposed of with contaminated medical waste.

Order and support

21. Where can I purchase the EMCOOLS cooling system?

The EMCOOLS products can be purchased directly from our distribution partners. Please refer to the "Distribution Network" section on our website for further details.

http://emcools.com/en/sales.aspx or http://emcools.com/de/vertrieb.aspx

22. Who do I contact if I need further clinical information and support?

If you require any further information or support do not hesitate to contact the EMCOOLS Team on emcools-office@emcools.com

REFERENCES

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Flex.Pad N is the commercial US-name of EMCOOLS Brain.Pad™.