Cardiothoracic Anesthesia, Respiration and Airway

Cerebral near-infrared spectroscopy in adult heart surgery: systematic review of its clinical efficacy

[La spectroscopie cérébrale par infrarouge en cardiochirurgie chez l'adulte : une étude systématique de son efficacité clinique]

Marie-Christine Taillefer PhD, André Y. Denault MD FRCPC

Purpose: This systematic review is aimed at answering the following questions: 1) Is near-infrared spectroscopy (NIRS) clinically effective in detecting cerebral desaturation during heart surgery? 2) Are these results based on studies with solid methodology?

Sources: MEDLINE, internet, and hand searches up to February 2004 for English and French papers on NIRS.

Principal findings: Forty-eight papers were retrieved, with a total of 5,931 cardiac surgery patients monitored by NIRS. More than 83% of patients underwent coronary artery bypass graft surgery. The majority of studies were prospective for the monitored group. Clinically, NIRS monitoring appears to detect brain desaturation episodes encountered during surgery. However, the majority of studies retrieved suffered from major methodological limitations and a low level of evidence. NIRS validity *vs* jugular bulb oximetry is questioned together with its predictive value in identifying those who will suffer postoperatively from neurological deficits. The sole randomized controlled trial appears to have recorded negative results in this respect.

Conclusion: The clinical application of NIRS in heart surgery as a brain-monitoring device seems interesting. However, NIRS has to be investigated more rigorously to prove its clinical utility in cardiac surgery.

Objectif : *Répondre à ces questions : 1) La spectroscopie par infrarouge (SPIR) est-elle efficace pour la détection clinique de la désaturation cérébrale en chirurgie cardiaque? 2) Les résultats sont-ils fondés sur une solide méthodologie des études?*

Sources : *MEDLINE, Internet et une recherche manuelle jusqu'en février 2004 pour les articles en anglais et en français sur la SPIR.*

Constatations principales : *Nous avons revu 48 articles, pour un total de 5 931 interventions en cardiochirurgie avec monitorage par la SPIR. Plus de 83 % des patients avaient eu un pontage aortocoronarien. La majorité des études avec monitorage étaient prospectives. Du point de vue clinique, le monitorage avec la SPIR permet de détecter les épisodes de désaturation cérébrale survenus pendant la chirurgie. Cependant, la majorité des études avaient d'importantes limites méthodologiques et un faible niveau de preuve. La validité de la SPIR vs l'oxymétrie du bulbe jugulaire est mise en question, ainsi que sa valeur prédictive à détecter les patients qui vont souffrir de déficits neurologiques postopératoires. Le seul essai randomisé et contrôlé avait des résultats négatifs à cet égard.*

Conclusion : *L'application clinique de la SPIR en cardiochirurgie comme moniteur cérébral semble intéressante. Cependant, la SPIR doit être étudiée plus rigoureusement si on veut prouver son utilité clinique en chirurgie cardiaque.*

NEUROLOGICAL complications and cognitive deficits are preoccupations in cardiac surgery because of their frequency, variety and long-term impact.[1–3] Disparities between prevalence and incidence can be explained by patient characteristics (age and comorbidities),[2,4–6] type of surgery,[4] differences in definitions of deficits, and how and when deficits are measured.[5]

From the Department of Anesthesiology, Montreal Heart Institute, Montreal, Quebec, Canada.
Address correspondence to: Dr. Marie-Christine Taillefer, Department of Anesthesiology, Montreal Heart Institute, Room R-2230, 5000 Belanger Street, Montreal, Quebec H1T 1C8, Canada. Phone: 514-376-3330, ext. 2043; Fax: 514-593-2160; E-mail: Marie-Christine.Taillefer@icm-mhi.org
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Brain activity monitoring during cardiac surgery is not new. Many techniques are available to monitor different aspects of brain activity: electroencephalogram (EEG), transcranial Doppler (TCD), brain saturation via jugular bulb oximetry ($SjVO_2$) or frontal cortex (ScO_2) near-infrared spectroscopy (NIRS).[7–18] The purpose of the present paper is to focus on NIRS.

This modality of neurological monitoring, a noninvasive brain saturation measurement tool, was introduced recently and approved in Canada.[12,13] Globally, NIRS is based on the absorption of infrared light by biological tissues in a fashion similar to arterial saturometry. The device employs two wavelengths (724 and 810 nm) to measure changes in the oxygenation of hemoglobin (Hb). The difference from conventional arterial saturation monitors is that NIRS has one transmitter and two receptors instead of one (Figure 1). The first receptor is located at 3 cm from the light source (transmitter); it captures the saturation level from extracerebral tissue (skin, bone, dura) and gives a superficial signal. The second receptor, placed more laterally at 4 cm from the light source, allows the analysis of a deeper signal from brain tissue. In the frontal position (Figure 2), it corresponds to the junction of the anterior and middle cerebral artery, in the so-called "watershed" territory. The device uses mathematical algorithms based on the modified Beer-Lambert law,[12,19,20] subtracting the superficial signal from the total signal to give only the value of the deep signal. In this cortical region, it is assumed that 75% of blood flow is composed of venous blood. Consequently, the final ScO_2 value will result in a balance between O_2 supply and consumption. The electrodes are connected to a computerized screen which gives real-time graphics of the saturation of both brain hemispheres from data gathered every ten seconds (Figures 1 and 2). Normal values for 250 awake preoperative CABG patients ranged from 47% to 83% (2 SD).[9]

This modality of cerebral monitoring is relatively new and promising for the prevention and correction of cerebral desaturation. However, no literature presents a global review of clinical outcome with cerebral oximetry and NIRS in cardiac surgery. Therefore, the present systematic review was undertaken. Our research questions were: 1) Is NIRS clinically effective in detecting cerebral desaturation during heart surgery? 2) Are these results based on studies with sound methodology?

Methods

Articles were retrieved by the authors (a post-doctoral fellow and a cardiac anesthesiologist) through different strategies. First, we screened bibliography on the Somanetics website: www.somanetics.com/bibliography.htm (last accessed in February 2004) for papers on NIRS in adult cardiovascular surgery. These references were linked to either PubMed, their journal home page, their meeting home page (abstracts), or PDF files. Second, we searched MEDLINE up to February 2004 with the following keywords: 1) "near infrared spectroscopy" alone and with "heart", "cardiac", "coronary artery bypass", "cardiac surgery", or "heart surgery" in the title, abstract, or review; 2) "near infrared oximetry" alone and with "heart", "cardiac", or "heart surgery" in the title, abstract, review; and 3) "cerebral oximetry" and "bypass" in the title. Third, the journal Cerebral Oximetry News (Summer 2001 issue) was reviewed. Finally, secondary references in the retrieved papers were screened. We excluded papers that were not written in English or French. No contact was made with authors to gather unpublished results. The data from each included paper were extracted by the first author (M.C.T.). Each study was also classified according to the levels of evidence proposed by Sackett[21] for evidence-based medical practice (Table I). Sackett's classification remains the most widely used today.[22]

Results

Results of literature search

A total of 417 papers were identified, from which 47 were deleted because they were not written in English or French. One hundred and sixty-four papers were not specific to cardiac surgery (n = 110) or studied

TABLE I Classification of levels of evidence[21]

Level of evidence	*Grade of recommendation*
Level I: Large randomized trials with clear-cut results (and low risk of error)	Grade A
Level II: Small randomized trails with uncertain results (and moderate to high risk of error)	Grade B
Level III: Nonrandomized, contemporaneous controls	
Level IV: Nonrandomized, historical controls	Grade C
Level V: No controls, case-series only	

Reproduced with permission from: *Sackett DL.* Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1989; 95(Suppl. 2): 2S–4S.

other populations such as pediatric cardiac surgery (n = 39), vascular surgery (n = 8), neurosurgery (n = 5), ventilated newborns (n = 1), and respiratory distress syndrome (n = 1). Sixty-two papers were not specific to cerebral infrared spectroscopy (n = 2) or studied other measurements or tests such as pulse oximetry (n = 43), continuous venous oximetry (n = 4), heart oxygen saturation (n = 4), jugular bulb oximetry (n = 2), blood gas oximetry (n = 2), catheters (n = 2), CO_2 challenge (n = 2), and Fick oximetry (n = 1). Sixty-seven papers described other measurements such as muscle oxygenation (n = 42) or described theoretical or fundamental research (n = 25). An additional 29 papers were excluded because they were duplicates (n = 22), published before 1970 (n = 4), or were letters or editorials (n = 3). A total of 48 clinical trials were left.[23–69] Table II summarizes these 48 studies and is available as Additional Material at www.cja-jca.org.

Description of studies

A total of 5,931 patients undergoing cardiac surgery have had their cerebral function monitored by NIRS. The vast majority (43/48; 89.6%) of studies retrieved were prospective with information on ScO_2 gathered during surgery and in the postoperative period. Only one study was a randomized controlled trial.[63] The remaining five studies (10.4%) were retrospective with information about ScO_2 gathered by chart review. None of the retrieved studies provided level I evidence. Only one (2.1%) was level II; four (8.3%) were level III; five (10.4%) were level IV, and 36 (75%) were level V. Two studies were classified as both levels III and IV; for one of these studies,[42] the decision was taken according to the type of control groups chosen, while for the other,[55] information available in the paper made it impossible to choose between both levels of evidence.

All studies were reporting on various cardiac operations, especially on-pump coronary artery bypass graft surgery (CABG; n = 30; 62.5%), followed by unspecified cardiac procedures (n = 11; 22.9%), valve surgery (n = 10; 20.8%), aortic arch procedures (n = 5; 10.4%), combined CABG and valve surgery (n = 4; 8.3%), off-pump CABG (n = 4; 8.3%), repair of atrial or ventricular septal defect (n = 3; 6.3%), CABG for patients at risk of stroke (n = 2; 4.2%), repair of tetralogy of Fallot (n = 1; 2.1%), and, finally, ventricular remodelling (n = 1; 2.1%). The percentages exceed 100% because many studies studied more than one procedure. Overall, at least 83% of the studies concerned CABG patients or closed heart surgeries. In all studies, saturation levels were not compared between open- and closed-heart surgeries.

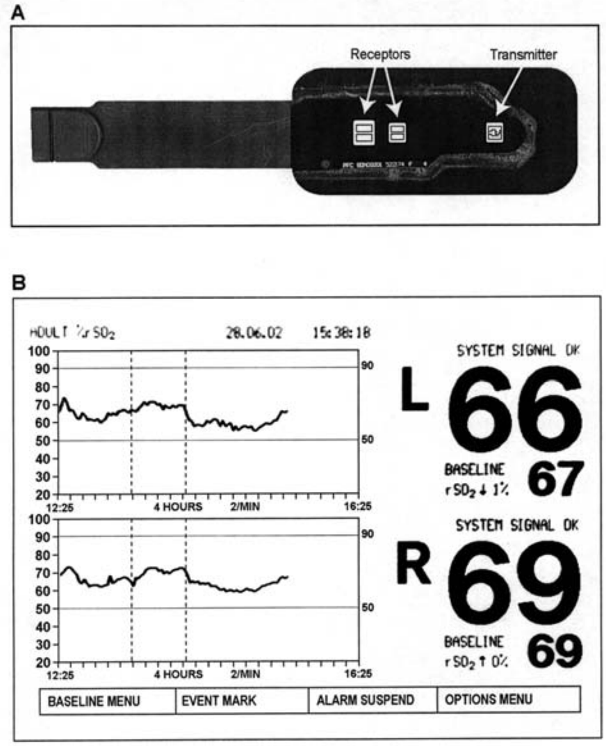

FIGURE 1 Examples of (A) an electrode and (B) realt-time graphics of brain saturation.

Among all papers retrieved, it appears that many models of NIRS technology were involved. Some deployed the INVOS 3100 (n = 3; 6.3%), the INVOS 3100A (n = 2; 4.2%), the INVOS 4100 (n = 5; 10.4%), the INVOS 5100 (n = 1; 2.1%), the NIRO 300 (n = 3; 6.3%), the NIRO 500 (n = 4; 8.3%), the RunMan (n = 1; 2.1%), and the NIRS model designed by some investigators[58] (n = 1; 2.1%). Others did not specify the model they used (n = 29; 60.4%).

Methodological quality of studies

The 48 included studies had diverse methodological characteristics and limitations. Biases arising from differences between the control and study groups included sample bias with heterogeneity amongst patients (n = 6; 12.5%), use of historical controls evaluated at an earlier time period (n = 6; 12.5%), and use of a retrospective design (n = 5; 10.4%). One study (2.1%) was unclear about the comparability of the groups. Three studies (6.3%) were case series. Inadequate power was a limitation in a number of studies either from small sam-

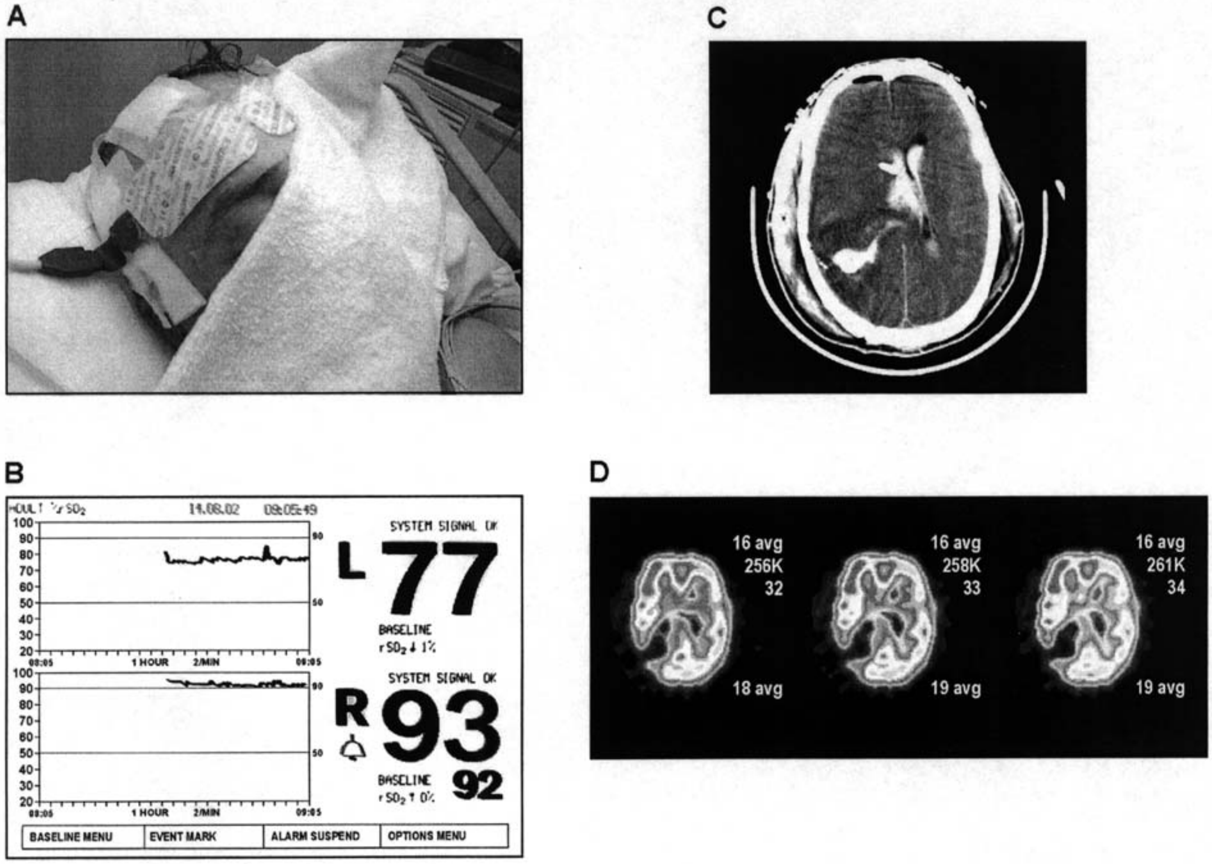

FIGURE 2 Examples of electrode placement on the forehead (A) and values of brain saturation due to mycotic aneurysm with cortical hemorrhage (B, C, D). The asymetrical distribution of the hemorrhage seen on the computed tomography scan (C) explains (D) the left to right discrepancy on the oximetry signal (B).

ple sizes (n = 18; 37.5%) or large differences between the numbers of patients in the control and study groups (n = 7; 14.6%). A number of factors limited the generalizability of the results including the recruitment of patients from only one centre (n = 47; 97.9%), selection of patients at high risk of neurological problems (n = 9; 18.8%), significant homogeneity of study patients with regards to gender (almost all males; n = 3; 6.3%), and the recruitment of patients from only one surgeon (n = 2; 4.2%). In two studies, neuropsychological evaluations were close together in time, which can bring regression of the results to the mean at subsequent evaluations (learning effect). Two-thirds of studies were published in abstract form (n = 28; 58.3%) with its inherent risk of reporting error. Finally, one study did not randomize flow patterns.[40]

Clinical efficacy of NIRS in heart surgery

According to the papers reviewed, the clinical efficacy of NIRS in cardiac surgery appears to be mixed. On the one hand, those who employed a cut point equivalent to a 20% decrease of the baseline value or a value < 50% before intervention to reverse desaturation obtained promising results.[37,39,41,44,53] Ganzel *et al.*, Alexander *et al.*, and Edmonds achieved success rates ranging from 93% to 100%.[45,52,55] Researchers have reported decreases in neurological complications,[45,52,55] incidence of renal failure,[45] other vital organ complications,[52] length of intensive care unit (ICU) stay,[38,44,51,62] total hospital stay,[38,42,44,51,52,55,62] and surgical costs[52,55] (Table II).

On the other hand, those who compared NIRS to $SjVO_2$ reported less encouraging results. While Kadoi *et al.*[34] found that NIRS was more effective in detecting brain desaturation than $SjVO_2$ at certain stages of normothermic and hypothermic CABG and suggested that one should not rely solely on $SjVO_2$ during cardiopulmonary bypass (CPB), others[24,27,48] considered NIRS less sensitive than $SjVO_2$. The sole randomized controlled trial[63] performed did not ascertain any difference in the number of neurological complications between patients who underwent NIRS monitoring and those who did not. In addition, two studies evaluated the ability of NIRS, using various cutoff values, to predict the incidence of neurological problems or the postoperative cognitive performance of patients, but did not find statistically significant differences between patients with NIRS measurements above or below the cutoff values.[26,60]

Discussion

NIRS has been deployed in cardiac surgery for 5,931 patients, of whom at least 83% were undergoing CABG. With the exception of one randomized controlled trial (level II evidence), every paper retrieved was level III to V evidence. However, NIRS validity has not been clearly established clinically along with its predictive value. In fact, the level of NIRS technological advancement led Bilfinger and Rampil[70] to question if signal variations were more significant for clinical purposes or for researchers.

In addition, the actual literature had numerous significant methodological limitations that precluded strong conclusions regarding the utility of NIRS brain monitoring technology in cardiac surgery. Caution must be taken particularly with abstracts. In fact, this form of publication delivers insufficient information and a higher risk of reporting errors, compared to peer-reviewed papers. In addition, eight of the most recent abstracts[45,55,56,63,65,66,68,69] were not published yet as full papers, although the full paper of the randomized controlled trial was in press[63] at the time of this systematic review. The small sample sizes and the non-randomized design in many of these studies further limit the strength of the evidence.

There were also technological limitations in regard to the advancement of NIRS devices. They mainly concerned: 1) absolute light absorption and scattering specific to each tissue,[9,12,13,70] 2) the volume of brain tissue exposed to the light source, 3) the resulting signal captured,[13] 4) the fact that different Hb species necessitate the use of other wavelengths,[9,70] 5) blood volume changes modifying transmission path length,[70] 6) possible displacement of the transmitter or receptors on the forehead,[12] 7) the influence of extracranial tissue (e.g., muscle) in the readings,[12] 8) differences between focal brain saturation and global measurements taken by $SjVO_2$ under CPB,[9] 9) inconsistency in the ratio between arterial/venous blood,[9] and, finally, 10) normal or near-normal saturation levels identified for dead or brain-dead patients.[9,71] This last aspect deserves further discussion because we have observed high values in brain-dead patients from the absence of infrared absorption. The value obtained in such situations is a more arterial type originating from the scalp. Similarly, jugular venous oxygenation will be elevated in these patients because blood originating from the jugular veins will somehow be arterialized, with no brain oxygen consumption occurring, as in hypothermia. Consequently, a normal to high value in an unknown or a newly-monitored patient might not reflect the true condition of brain oxygenation. Maeda *et al.*[72] emphasized the limited utility of post-mortem oximetry since severe systemic hypoxia is a common final state before death in many traumas and diseases.

Another important finding extracted from this systematic review is that there are many diverse models of NIRS technology. Common to all NIRS technology is the fact that light is generated at specific wavelengths and a computer converts the change in light attenuation to modifications in chromophore concentration.[20] However, as described by Owen-Reece *et al.*,[20] there are two different methods of data handling: non-quantitative measurement, as with INVOS technology, and quantitative concentration measurement, as with NIRO technology. The former measures the ratio of light absorption by oxyhemoglobin (HbO_2) and total Hb and calculates from it a value for mean cerebral saturation. The latter is a combination of multi-distance measurements of optical light attenuation, with several detectors calculating the relative concentration of Hb and HbO_2 in illuminated tissue, which gives an estimate of mean tissue Hb saturation. This information may influence comprehension of the review results, knowing, in addition, that many authors had not specified the NIRS model they used. Reviews[7,8,15,52,73] usually recommend cerebral oximeters with other monitoring modalities (EEG, TCD, bispectral index) to identify and correct numerous threats to patients' brains. However, Dujovny *et al.*[11] suggest that neither non-invasive nor invasive brain monitoring techniques are universally accepted.

Despite its limitations, monitoring of brain saturation appears desirable to allow interventions before long-term neurological deficits occur.[70] Those undergoing CABG, particularly if they are elderly, represent a high-risk population. Some studies[41,61,63,64] have been performed in this population. A few authors[31,47] have suggested that brain monitoring could be beneficial, particularly for patients submitting to cardiac surgery under circulatory arrest. However, this hypothesis was not confirmed in a study[64] that found no significant results with NIRS in such a setting. Severe neurological complications, death, or days-from-surgery-to-discharge were not different in monitored patients compared to those who were not.

While these complications do not necessarily persist in the long-term, it is estimated that worldwide almost half a million patients undergoing CABG annually will suffer persistent cognitive decline.[3] In a prospective study, Newman *et al.*[3] established that cognitive decline at discharge from hospital after surgery was a risk factor for persistent cognitive decline five years later. Another risk factor for neurological and cognitive deficits after heart surgery is advanced age.[2,4–6] With increased life expectancy of the population and the fact that heart surgery is being performed on patients who are getting older, the prevalence of these complications will probably rise further. Consequently, methods to detect and correct brain dysfunction have been developed.

NIRS has many other advantages over conventional saturometry. First, data on local oxygenation and perfusion can be obtained, allowing the detection of focal brain damage, which is impossible with $SjVO_2$. Second, it is particularly interesting in the extracorporeal circulation because a pulsatile signal is not required. The technique has also been validated against many other modalities of brain monitoring: in jugular saturometry,[74] for the measurement of brain output,[12] and in numerous contexts, such as adult and pediatric cardiac surgery, neurosurgery, dysoxia in newborns and fetuses, in the ICU and interventional cardiology.[7–13,15,52] Therefore, when ScO_2 value declines, it is by itself an indication of brain desaturation.

Another possible advantage of NIRS technology in cardiac surgery is its potential cost-efficacy ratio. In fact, it is estimated that each neurological deficit in a patient costs about $15,000 US, while monitoring itself (monitor, electrodes) costs about $375 US per patient.[75] Similarly, Edmonds *et al.*[33] have demonstrated that unmonitored patients stayed on average 43 hr more in the ICU, representing cost-savings of $3,569 US per patient (43 hr × $83 US per hour), which is almost ten times the cost of the device. Ganzel *et al.*[55] anticipated an 11% decrease in average hospital costs because of monitoring. Schmahl[42] estimated that routine monitoring would reduce hospital costs by more than 10% or $1,500,000 US.

Finally, our systematic review has its own limitations. We have not contacted authors to gather unpublished material regarding the use of brain saturation devices in heart surgery and we have excluded papers that were not published in English or French. In addition, we have not included every type of surgery, especially those, such as endarterectomy, performed at the same time as cardiac surgery.

Conclusions

Many studies presented in this systematic review tend to report positive results regarding the clinical efficacy of NIRS in cardiac surgery. However, most of them have major methodological limitations and a low level of evidence. In addition, its superiority to $SjVO_2$ and its predictive validity has not yet been fully demonstrated clinically. NIRS appears to be a promising technology, but more research is needed to establish its clinical efficacy and justify its routine use during cardiac surgery.

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