

# Stellenwert des Cell-Savers im Patient-Blood-Management

IAKH Ludwigshafener Transfusionsgespräche 28.-29.März 2014

Georg Bonnländer

Bad Abbach



Sylt



Barmbek (Hamburg)



Falkenstein



Ini Hannover



Bad Griesbach

Interessensdeklaration: Vortragshonorare von der Fa. Sorin, München

# Vorstellung: Asklepios-Klinikum Bad Abbach

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Lehrstuhl für Orthopädie der Universität Regensburg

Ca. 4000 – 4500 operative Eingriffe

Komplettes operatives Spektrum

Ca. 1400 – 1500 Endoprothesen

Dabei ca. 1200 endoprothetische Primäreingriffe

Sieben Anästhesisten, davon sechs Fachärzte

Anästhesie stellt den Transfusionsverantwortlichen, einen Transfusionsbeauftragten und den Qualitätsbeauftragten

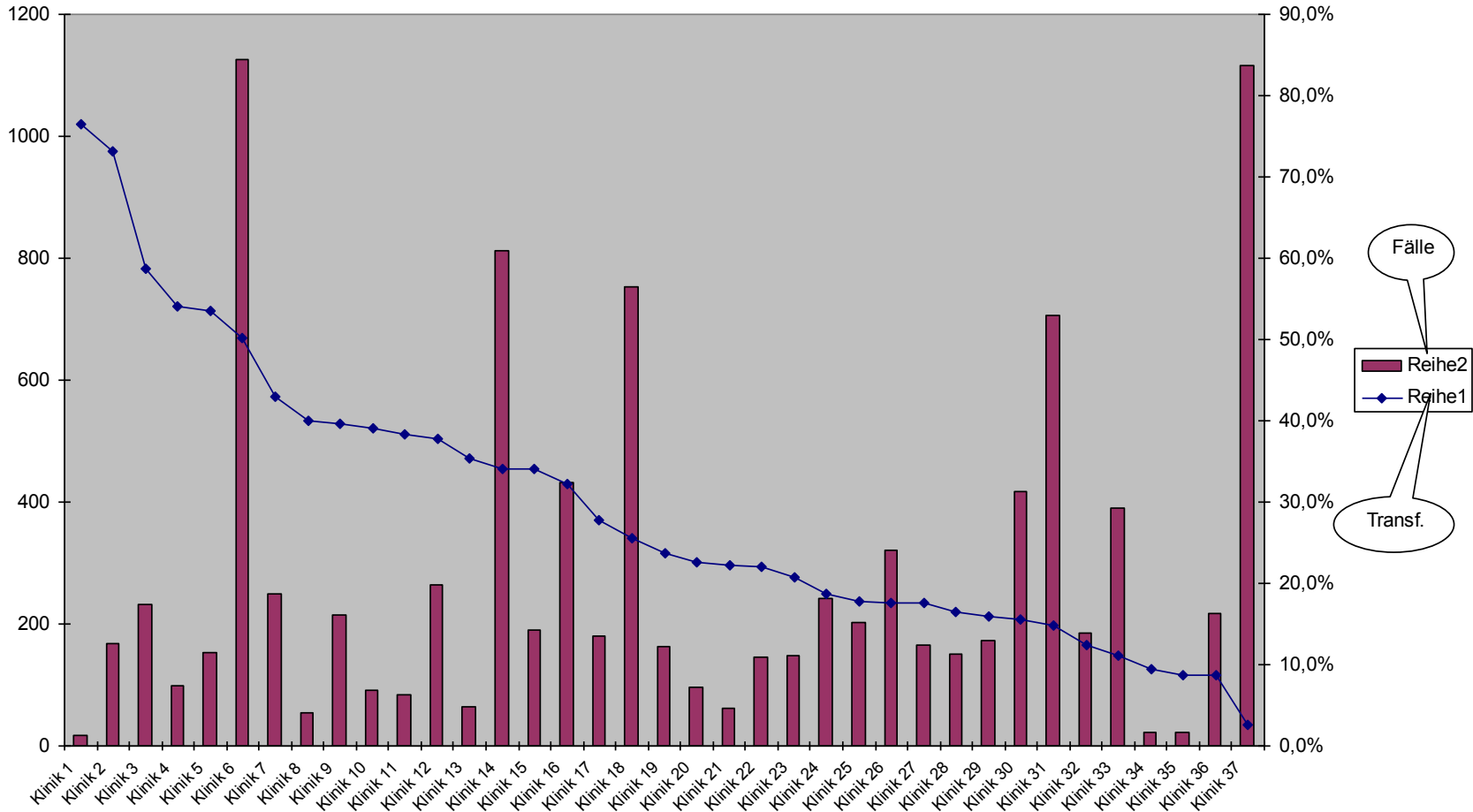
AWR / ICU mit 14 Betten 24 h besetzt

Fünf MAT – Geräte im Einsatz

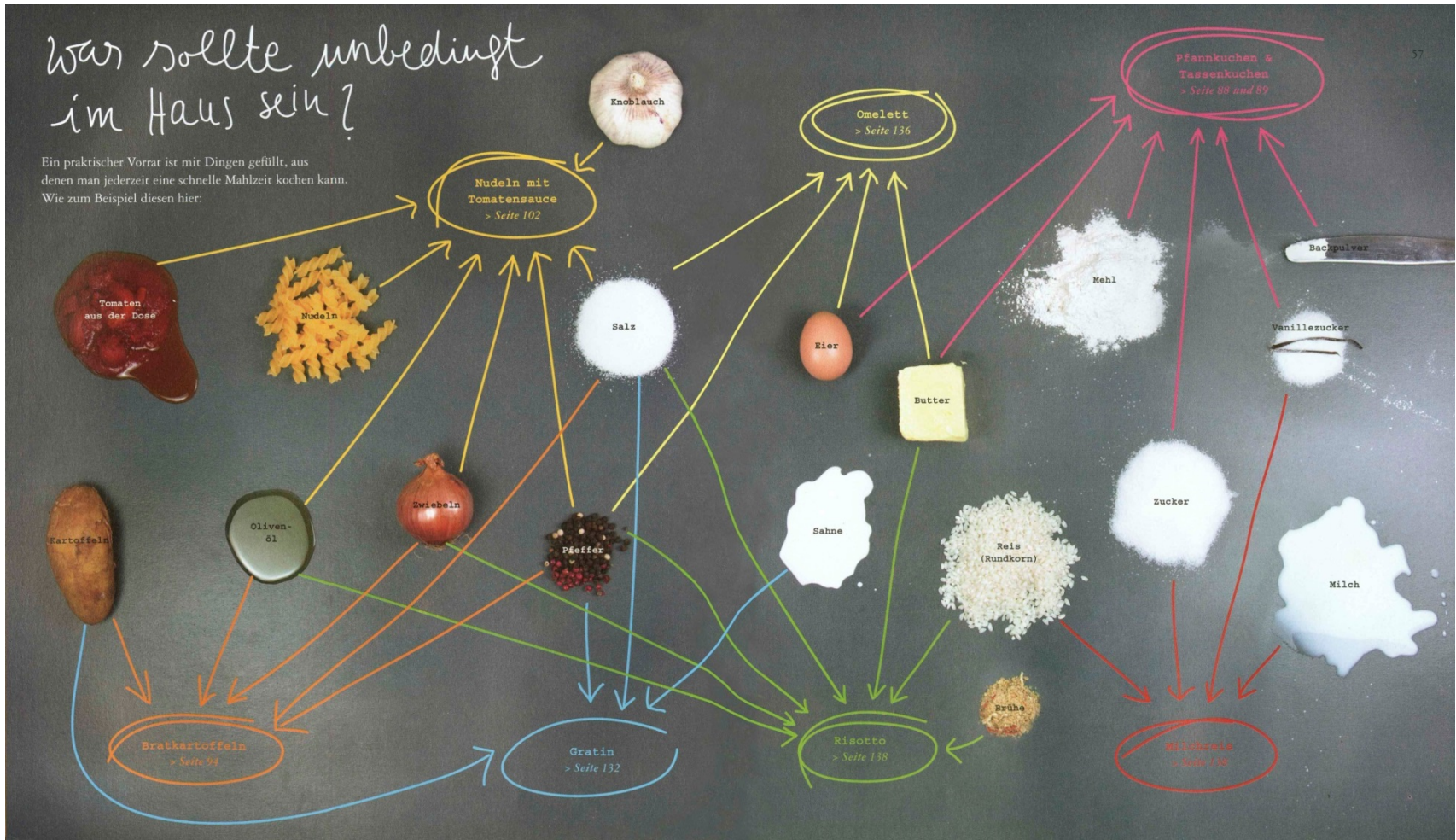
Ca. 1000 Reservoire pro Jahr, ca. 700 Waschsets

**Transfusionswahrscheinlichkeit primäre Endoprothetik 2013**

**Knie-TEP: 1,2 % Hüft-TEP 1,4 %**



Transfusionswahrscheinlichkeit versus operative Fallzahl primäre Endoprothetik 2010



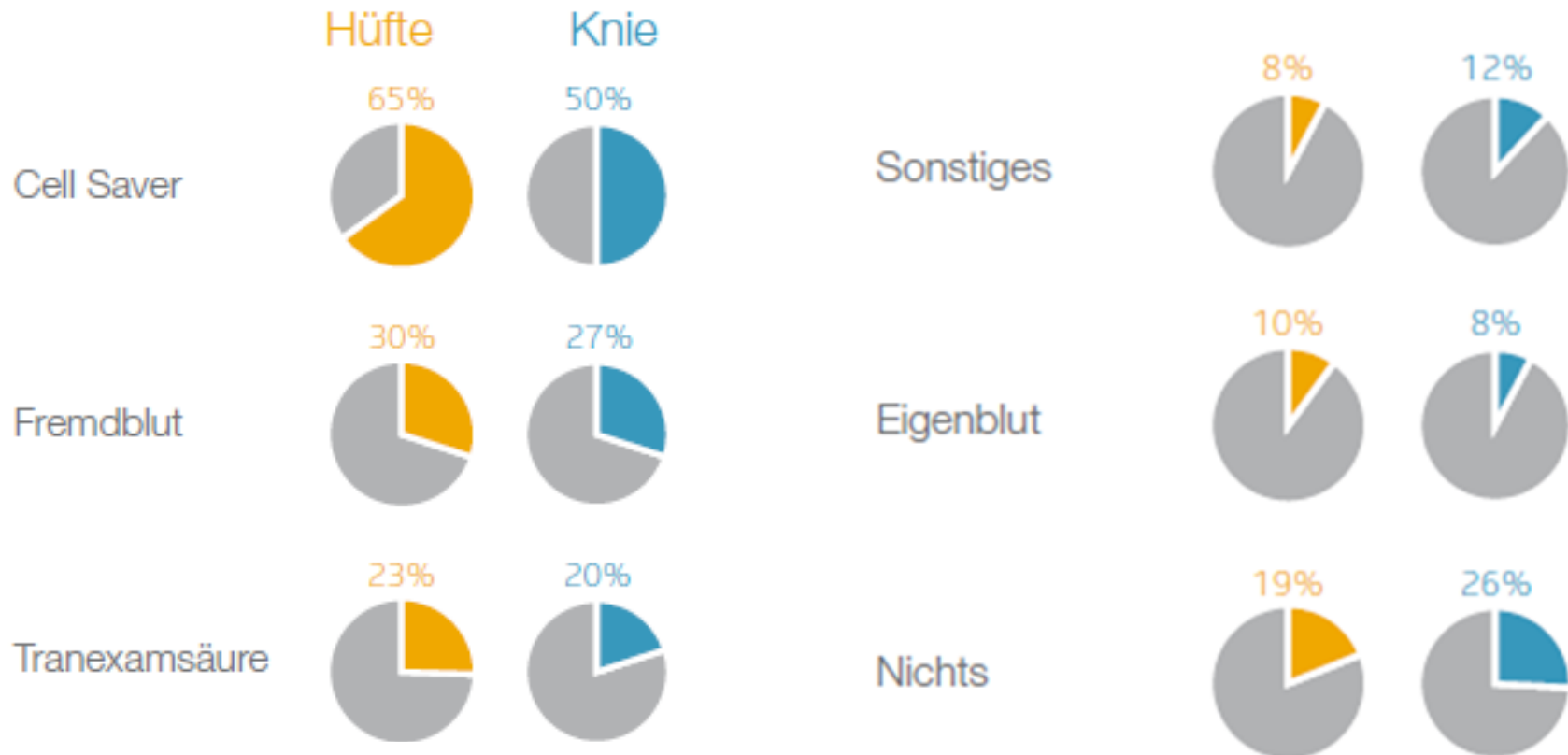
Umgesetzte Maßnahmen am ASKLEPIOS-Klinikum Bad Abbach:

- Optimierung des präoperativen Hämoglobinwertes
- Option der präoperativen Eigenblutspende
- Temperatur-Management
- Regionalanästhesie
- kontrollierte Hypotension
- adrenalinaugmentierte hypotensive Periduralanästhesie
- Gerinnungs-Management
- pH-Management
- Anämietoleranz
- Maschinelle Autotransfusion („Cellsaver“)





## Blutmanagement bei Hüft- und Knieoperationen (1. Berliner Orthopädie-Report 2013)





# Patient Blood Management: Limitierungen

Optimierung des präoperativen Hämoglobinwertes:

- Hoher logistischer Aufwand
- fehlende Compliance von Patienten und Kollegen
- Erythropoetin (fraglich erhöhte Mortalität, kardiovaskuläre Ereignisse, vermehrte Tumorprogression) Evidenzgrad 2A
- Eisen (essentiell für Tumorwachstum, erhöhte Infektionen) Evidenzgrad 1B

Option der präoperativen Eigenblutspende:

- Zeitnot, Anämie, KM-Insuffizienz,
- Risiken (Verwechslung, Lagerungsschäden),
- hohe Ausschussrate

Anämietoleranz Evidenzgrad 1A

**EJA**

*Eur J Anaesthesiol* 2013; **30**:270–382

## GUIDELINES

### **Management of severe perioperative bleeding**

*Guidelines from the European Society of Anaesthesiology*

How can we explain the gap between randomised studies and 'real life' practice in postoperative transfusion triggers?  
Do we need to change recommended thresholds for transfusion?

Nadia Rosencher, Yves Ozier, Francois Souied, Andre' Lienhart and Charles-Marc Samama

European Journal of Anaesthesiology 2012, 29:460–461

- Anaesthetic procedures :7756 121 per year
- Total of 419 deaths totally or partly related to anaesthesia
- Nearly 100 deaths occur perioperatively in France every year as the result of inadequate blood management

We should not manage anaemia in the recovery room and at postoperative day 5 in the same way. Sometimes, according to the kinetics of bleeding, the transfusion trigger should be different in the recovery room and in the ward.

# Patient Blood Management

Was sollte unbedingt im Haus sein?

Ein praktischer Vorrat ist mit Dingen gefüllt, aus denen man jederzeit eine schnelle Mahlzeit kochen kann. Wie zum Beispiel diesen hier:



## **Maschinelle Autotransfusion im PBM:**

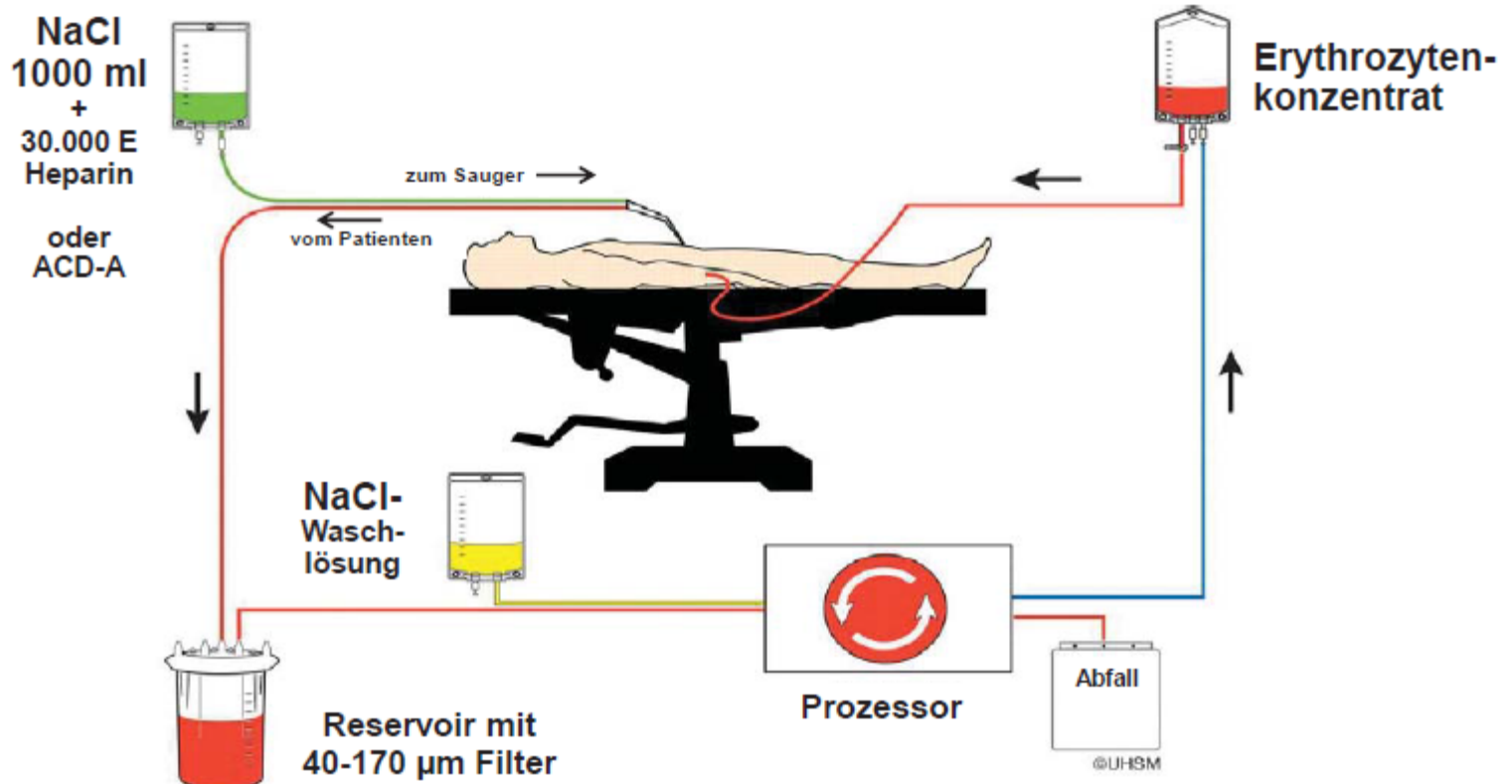
**„Die Erythrozyten dort retten, wo sie sonst verloren gehen !“  
(Cell-Saver)**

- Chirurg: „Das blutet nicht.“  
Später:“ Blutung war nicht absehbar.“
- Transfusionsmediziner: „Unser Blut ist so sicher,  
wir brauchen keine Alternative.“
- Anästhesist: „MAT ist Routine, da gibt es nichts Neues.“  
„MAT lohnt sich erst ab 1 l Blutverlust.“

Die Wertigkeit der MAT ist in der Klinik nicht bewusst !



## Intraoperative Maschinelle Autotransfusion



TiKuppurao L , Wee M Contin Educ Anaesth Crit Care Pain 2010;10:104-108, verändert nach UK Cell Salvage Action Groupation



ELECTA, CS5

Latham bowl



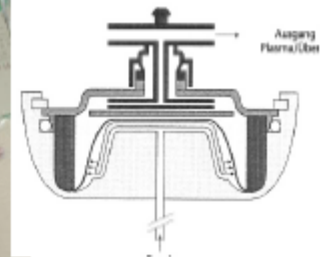
CATS

continuous



OrthoPAT

flexible disc



**Maschinelle Autotransfusion**  
**Hansen E.; Seyfried T.**  
**Der Anaesthesist 2011;60(4):381-390**

Blutverlust gesammelt  
im Reservoir: 60-70%

Erythrozyten-Ausbeute  
Beim Zellwaschen: 80-90%



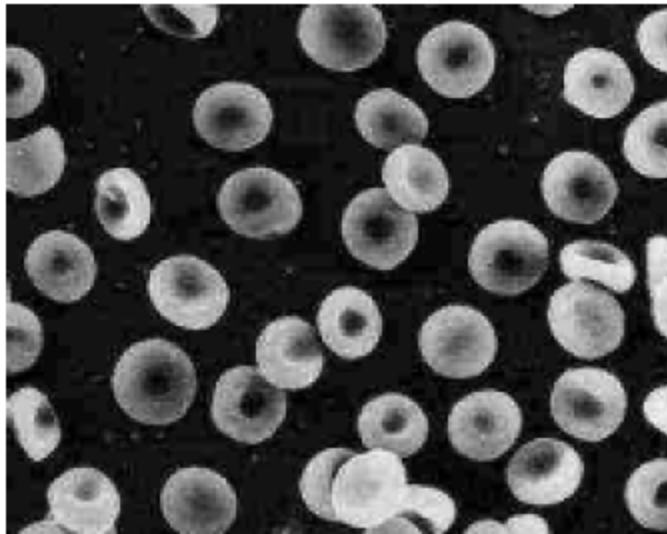
**Mindestens 50% der Erythrozyten  
des Blutverlustes werden  
retransfundiert**

z.B. in der Orthopädie ([Hansen et al. 1983](#))

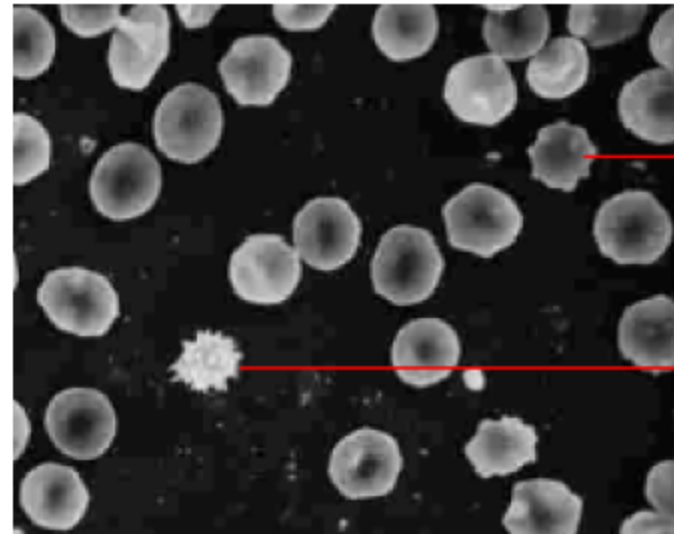


**äquivalente (ca. 50%) Einsparung  
an Fremdbluttransfusion**

## Salvaged Blood



## Banked Blood



Deformability	107	49
Normal morphology (%)	93	35

	<b>Banked Blood</b>	<b>Salvaged Blood</b>
<b>pH</b>	6.73	7.52
<b>K+</b> (mmol/L)	47.2	1.2
<b>2,3DPG</b> (μmol/gHb)	0.7	13.8
<b>fHb</b> (g/L)	1.6	0.3
<b>ATP</b> (μmol/gHb)	2.3	4.3
<b>24h survival</b> (%)	79.7	94.7
<b>Citrate</b> (mol/L)	15.2	0

## **Erythrozyten**

- **autolog** (nicht immunogen, nicht antigen,  
nicht immunosuppressiv)
- **frisch** (ungelagert, ungekühlt)
- **volle Funktionsfähigkeit**
- **hohe Vitalität** (Überleben nach Transfusion)
- **gewaschen**

**= ein Blutprodukt höchster Qualität  
für eine optimale Hämotherapie**



## Modulares Vorgehen in der Klinik: Großzügige Indikation zum Reservoir-Einsatz

Die Entscheidung bezüglich der Aufbereitung des Wund/Drainagenblutes kann nicht alleine vom gesammelten Volumen abhängig gemacht werden. In diese Entscheidung fließen ein:

- das berechnete Ausgangsblutvolumen des Patienten vor dem Eingriff,
- die Gerinnungssituation,
- die Dynamik des bisherigen Blutverlustes,
- der postoperative Hb-Wert,
- das bisher gefahrene Infusionsregime,
- Begleiterkrankungen des Patienten,
- Verfügbarkeit von Erythrozytenkonzentraten und AK-Situation,
- erfahrungsgemässes weiteres Absinken des Hb-Wertes postoperativ,
- Erwartungshaltung des Patienten.

## Klassische Indikationen der MAT

Evidenzgrad 1A für:

- Traumatologie
- Orthopädie
- Herzchirurgie
- Gefäßchirurgie

Kontraindikationen ?!?

- Visceralchirurgie
- operative Geburtshilfe
- Tumorchirurgie

*British Journal of Anaesthesia* **105** (4): 401–16 (2010)  
Advance Access publication 28 August 2010 · doi:10.1093/bja/aeq244

BJA

## REVIEW ARTICLES



# Cell salvage as part of a blood conservation strategy in anaesthesia

A. Ashworth and A. A. Klein\*

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**EJA**

*Eur J Anaesthesiol* 2013; **30**:270–382

## GUIDELINES

### **Management of severe perioperative bleeding**

#### *Guidelines from the European Society of Anaesthesiology*

Sibylle A. Kozek-Langenecker, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa Alvarez Santullano, Edoardo De Robertis, Daniela C. Filipescu, Dietmar Fries, Klaus Görlinger, Thorsten Haas, Georgina Imberger, Matthias Jacob, Marcus Lancé, Juan Llau, Sue Mallett, Jens Meier, Niels Rahe-Meyer, Charles Marc Samama, Andrew Smith, Cristina Solomon, Philippe Van der Linden, Anne Juul Wikkelsø, Patrick Wouters and Piet Wyffels

Table 1 Grades of recommendation – GRADE system

	Clarity of risk/benefit	Quality of supporting evidence	Implications
<b>1A Strong recommendation. High quality evidence.</b>	Benefits clearly outweigh risk and burdens, or vice versa.	Consistent evidence from well performed randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendation, can apply to most patients in most circumstances without reservation.
<b>1B Strong recommendation. Moderate quality evidence.</b>	Benefits clearly outweigh risk and burdens, or vice versa.	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation, likely to apply to most patients
<b>1C Strong recommendation. Low quality evidence.</b>	Benefits appear to outweigh risk and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain.	Relatively strong recommendation; might change when higher quality evidence becomes available
<b>2A Weak recommendation. High quality evidence.</b>	Benefits closely balanced with risks and burdens.	Consistent evidence from well performed, randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values.
<b>2B Weak recommendation. Moderate quality evidence.</b>	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens.	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances
<b>2C Weak recommendation. Low quality evidence.</b>	Uncertainty in the estimates of benefits, risks and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable

Kontraindikation Visceralchirurgie ?

Risiko Kontamination mit Darminhalt

RCT : 44 Fälle, penetrierendes Bauchtrauma

92% nach dem Waschen positiv: Kein Zusammenhang der positiven BK mit postoperativen Infektionen.

Beobachtungsstudien: >150 Fälle, penetrierendes Bauchtrauma. Kein Anstieg postoperativer Infektionen.

Ozman V et al. Autotransfusion of potentially culture-positive blood in abdominal trauma: preliminary data from a prospective study. J Trauma 1992; 32: 36-9.

Timberlake GA, McSwain NE. Autotransfusion of blood contaminated by enteric contents: a potentially lifesaving measure in the massively hemorrhaging trauma patient. J Trauma 1988; 28: 855-7.



Kontraindikation Visceralchirurgie ?

Risiko Kontamination mit Darminhalt

We recommend that intraoperative cell salvage is not contraindicated in bowel surgery, provided that initial evacuation of soiled abdominal contents and additional cell washing are performed, and that broad-spectrum antibiotics are used. 1C

Eur J Anaesthesiol 2013; 30:270–382

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker et al.

## **Kontraindikation: operative Geburtshilfe ?**

## **Problemstellung: Amnionflüssigkeit, fetale Erythrozyten**

MAT erhöht weder die Rate der Fruchtwasserembolien, noch der Infektionen oder der DIC.

MAT reduziert signifikant die Fruchtwassermenge.

Fetale Erythrozyten werden zwar weder ausgewaschen noch abgefiltert, das mütterliche Immunisierungsrisiko ist nicht höher als bei vaginaler Entbindung.

Geoghegan J et al. Cell salvage at caesarean section: the need for an evidence-based approach. Br J Obstet Gynaecol 2009;116: 743–7

Allam J et al. Cell salvage in obstetrics. Int J Obstet Anaesth 2008; 17: 37–45

Sullivan I et al. Contamination of salvaged maternal blood by amniotic fluid and fetal red cells during elective Caesarean section. Br J Anaesth 2008; 101: 225–9

## **Kontraindikation: operative Geburtshilfe ?**

## **Problemstellung: Amnionflüssigkeit, fetale Erythrozyten**

MAT in der Geburtshilfe ist sicher und wird empfohlen : Evidenzgrad 1C

NICE fordert zusätzlich Leukozytendepletionsfilter

Intraoperative cell salvage in obstetrics: is it a real therapeutic option? Transfusion 2011 Liunbruno GM et.al  
OAA/AAGBI Guidelines for Obstetric Anaesthetic Services. Revised Edition: OAA/AAGBI, London; 2005. S. 25

Why mothers die. Confidential Enquiry into Maternal and Child Health 2000-2002. London, RCOG, 2004

CEMACH, <http://cmace.org.uk/Publications/CEMACH-Publications/Maternal-and-Perinatal-Health.aspx>

National Institute for Health and Clinical Excellence. Intraoperative Blood Cell Salvage in Obstetrics, 144. 2005. <http://guidance.nice.org.uk/IPG144>

*Should cell salvage be used in obstetrics?*

**Recommendations**

*Cell salvage is well tolerated in obstetric settings, provided that precautions are taken against rhesus isoimmunisation. C*

## Kontraindikation Tumorchirurgie ?

Tumorchirurgie: spezielle Problematik

- $\frac{1}{4}$  aller Blutkonserven in Deutschland für diese Patientengruppe (Anämie hat bei diesen Patienten direkten Einfluss auf Tumorrezidiv und Überleben und beeinträchtigt die Wirkung von Chemo- und Bestrahlungstherapie).
- Transfusionsrisiken sind in dieser Patientenpopulation besonders belastend (die transfusionsbedingte Immunmodulation (TRIM))
- Fremdblutgabe hat negative Folgen auf die Tumorkrankheit und verringert die Überlebenschancen durch höhere Rezidivraten und Metastasierung

## **Tumorchirurgie**

### Gynäkologische Eingriffe mit MAT Evidenzgrad 1C

#### Recommendation

Cell salvage may reduce allogeneic transfusion in gynaecological (including oncological) surgery.

Increasing evidence supports the use of filters to clear shed blood of cancer cells, avoiding reinfusion and dissemination. Retrospective studies suggest that cell salvage reduces allogeneic transfusion requirements.

Eur J Anaesthesiol 2013; 30:270–382

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker et al.



## **Tumorchirurgie**

### Lebertransplantation / Teilresektion

UK guidelines state that ICS may be considered for hepatocellular tumor surgery if there is a significant risk of major bleeding. Risk of malignant cell reinfusion should be balanced against risk of allogenic transfusion-related complications, Leukodepletion filters reduce reinfusion risks.

Eur J Anaesthesiol 2013; 30:270–382

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## **Tumorchirurgie**

Studies in urological cancer surgery have shown ICS not to affect biochemical recurrence or long term survival. In 2008, the UK National Institute of Health and Clinical Excellence (NICE) approved the use of ICS in urological malignancy surgery.

Eur J Anaesthesiol 2013; 30:270–382

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker et al.

## Blood salvage and cancer surgery: ameta-analysis of aviable studies

Transfusion 2012 Oct.

Waters JH et al.

Elf Studien; 2356 Patienten; Leber-, Pankreas-, Cervix- und gastrointestinale Carzinome

Conclusions: While significant variability existed between studies, this meta-analysis suggests that outcomes after the use of ISB are not inferior to traditional intraoperative allogeneic transfusion

## **Should intraoperative cell-salvaged blood be used in patients with suspected or known malignancy?**

Jacqueline D. Trudeau, MD, PhD • Terrence Waters, MD • Kate Chipperfield, MD

Canadian Anesthesiologists' Society September 2012

### Abstract

Intraoperative cell salvage (ICS) is used as alternative to allogeneic blood transfusion in an attempt to avoid or minimize the risks associated with allogeneic blood. Intraoperative cell salvage is generally avoided in surgeries where malignancy is confirmed or suspected due to concern for potential metastasis or cancer recurrence. The application of post-processing methods for ICS is hypothesized to eliminate this potential risk. The purpose of this narrative review is to examine the in vitro experimental evidence as it pertains to the removal of tumour cells from ICS blood and to review the clinical studies where ICS blood has been used in patients with malignancy.

Source A search of the English literature for relevant articles published from 1973 to 2012 was undertaken using MEDLINE and Cochrane databases. Bibliographies were cross-referenced to locate further studies.

Principal findings: Leukoreduction filters are an effective method for removal of malignant cells from ICS blood.

Small non-randomized clinical studies to date do not show evidence of an increased rate of metastasis or cancer recurrence. Although a theoretical risk of disease recurrence persists, the decision to use autologous ICS blood must be weighed against the known risks of allogeneic blood transfusion.

Conclusion Transfusion of autologous blood harvested via ICS should be considered a viable option for reduction or avoidance of allogeneic product during many oncologic surgeries and may be a lifesaving option for those patients who refuse allogeneic blood products

It is reasonable to conclude that the risk associated with autotransfusion of a small number of potentially tumourigenic cells from the operative field is negligible, as many cancer patients already have a significant number of circulating cancer cells prior to surgery.<sup>37-41</sup> It is thought that tumour cells are released continuously in a regulated balance between tumour and host. Indeed, the median number of tumour cells released into the renal vein of patients with primary renal cancer has been estimated at 37 million per day.<sup>42</sup> These cells are felt to be viable and potentially tumourigenic as they are freshly released into a major blood vessel from the tumour site. However, the ability of circulating tumour cells to form metastases is low, a concept that has been termed “*metastatic inefficiency*”.<sup>43</sup> Based on animal studies, it has been estimated that as few as 0.01-0.000001% of disseminated cancer cells have the ability to form metastatic lesions.<sup>43</sup>

When ICS is used for oncologic surgery, harvested red blood cell concentrates do contain a significant number of malignant cells. Despite this, the evidence to date does not show an increased risk of tumour recurrence or metastasis as a result of using ICS during oncologic surgery. A large body of evidence suggests that the safety of ICS blood can be improved further when used for cancer surgery with the subsequent use of an LR filter or irradiation. The majority of evidence, together with ease of use, has resulted in a recommendation for LR filters (over irradiation) in new practice guidelines.

## Cancer Research

Published OnlineFirst March 5, 2014; doi: 10.1158/0008-5472.CAN-13-1885

## Immune Escape and Survival Mechanisms in Circulating Tumor Cells of Colorectal Cancer

[Gunnar Steinert<sup>1</sup>](#), [Sebastian Schölch<sup>4</sup>](#), [Thomas Niemietz<sup>1</sup>](#)

### Abstract

The prognosis of colorectal cancer is closely linked to the occurrence of distant metastases. Systemic dissemination is most likely caused by circulating tumor cells (CTC)... Several CTC exhibited mutations in key genes such as *KRAS* or *TP53* that could not be detected in the tumor. ... Gene expression analyses revealed both a pronounced upregulation of *CD47* as a potential immune-escape mechanism and a significant downregulation of several other pathways, suggesting a dormant state of viable CTC. Our results suggest mutational heterogeneity between tumor tissue and CTC that should be considered in future trials on targeted therapy and monitoring of response.

## Anesthesiology

**Issue: Volume 114(2), February 2011, pp 283-292**

### **Association between Intraoperative Blood Transfusion and Mortality and Morbidity in Patients Undergoing Noncardiac Surgery**

**Glance, Laurent G. M.D.\***; Dick, Andrew W. Ph.D.†; Mukamel, Dana B. Ph.D.‡; Fleming, Fergal J. M.D.§; Zollo, Raymond A. M.D.\*; Wissler, Richard M.D.\*; Salloum, Rabih M.D.[//]; Meredith, U. Wayne M.D.#; Osler, Turner M. M.D.\*\*

This was a retrospective analysis of the association of blood transfusion and 30-day mortality and 30-day morbidity in 10,100 patients undergoing general, vascular, or orthopedic surgery.

Results: Intraoperative blood transfusion was associated with an increased risk of death (odds ratio [OR], 1.29; 95% CI, 1.03–1.62). Patients receiving an intraoperative transfusion were more likely to have pulmonary, septic, wound, or thromboembolic complications, compared with patients not receiving an intraoperative transfusion. Compared with patients who were not transfused, patients receiving one or two units of erythrocytes were more likely to have pulmonary complications (OR, 1.76; 95% CI, 1.48–2.09), sepsis (OR, 1.43; 95% CI, 1.21–1.68), thromboembolic complications (OR, 1.77; 95% CI, 1.32–2.38), and wound complications (OR, 1.87; 95% CI, 1.47–2.37).



## Anesthesiology

Issue: Volume 114(2), February 2011, pp 234-236

### More on Transfusion and Adverse Outcome: It's Time to Change

**Spahn, Donat R. M.D., F.R.C.A.\*; Shander, Aryeh M.D., F.C.C.P., F.C.C.M.†; Hofmann, Axel M.E.‡; Berman, Mitchell F. M.D., M.P.H.§**

Contrarians to the above still overly rely on banked blood products, despite mounting evidence that patient blood management is achievable, avoids exposure to allogeneic blood products, improves patient outcome, and saves resources. **The ease of ignoring preoperative anemia as well as the simplicity of ordering and transfusing RBCs and thereby completely ignoring the burgeoning evidence of adverse transfusion outcome are not in the best interest of patients. Maintaining the clinical status quo under such circumstances would not be accepted in any other field of medicine in the context of current safety and quality standards.**

Working on studies regarding benefit or detriment of allogeneic RBC transfusions is important, but more so is acting already today according to patient blood management principles; **it is time for a change toward better patient care.**

Die Etablierung eines suffizienten Patient Blood Management kristallisiert sich zu einer der großen Herausforderungen in der operativen Medizin in den kommenden Jahren.

Die einzelnen Bausteine des PBM dürfen in ihrer Effizienz allerdings nicht überschätzt werden.

Eine konsequente Umsetzung ist sehr aufwendig und wird den gleichen Entwicklungsweg wie die heutige „Akutschmerztherapie“ beschreiten müssen.

Der zentrale Baustein im PBM ist dabei die Maschinelle Autotransfusion als effektive und sichere Technik, die schnell und günstig mindestens 50 % des verlorengegangenen Erythrozytenvolumens mit höchster Qualität wieder bereitstellen kann. Es ist einfach naheliegend, das Blut unmittelbar dort wiederzugewinnen, wo es verlorengeht.

Dazu bietet sich ein modulares Vorgehen an: Großzügig sammeln, aber nur dann aufbereiten, wenn es indiziert ist. Die organisatorischen und auch räumlichen Kapazitäten sind dafür unverzichtbar.

(Genügend Platz im Aufwachraum, ggf. Intermediate Care Unit, geschultes Personal).

Dringend notwendig ist eine neue Indikationsstellung des MAT – Einsatzes außerhalb der klassischen Indikationen: MAT auch bei onkologischen, abdominalchirurgischen Eingriffen und Geburtshilfe.

Die Hersteller der MATs sind gefordert, Leucozytendepletionsfilter in ihren Waschsets zu integrieren.

Die Querschnittsleitlinien müssen überprüft werden.

It's Time to Change !





Ihr Handy muss auf jeden Fall nicht verschlüsselt werden.  
Was Sie so reden, ist kryptisch genug!

SZ-ZEICHNUNG: DIRK MEISSNER



Vielen Dank für Ihre Aufmerksamkeit !