SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Reggio Emilia
IRCCS Istituto in tecnologie avanzate e modelli assistenziali in oncologia

OECI CLINICAL Cancer Centre

Recupero intraoperatorio in oncologia

Chiara Marraccini, PhD

PBM
organizzazione, clinica
e scenari futuri

Cesena Fiera
Sala Malatesta Novello
28 - 29 Marzo 2019

Dichiarazione sul Conflitto di Interessi

Non ho alcun coinvolgimento o interesse che possa far sorgere il problema di una distorsione nella presentazione, nel lavoro, nelle conclusioni o nelle opinioni espresse nella mia presentazione.

Cochrane Library
Cochrane Database of Systematic Reviews

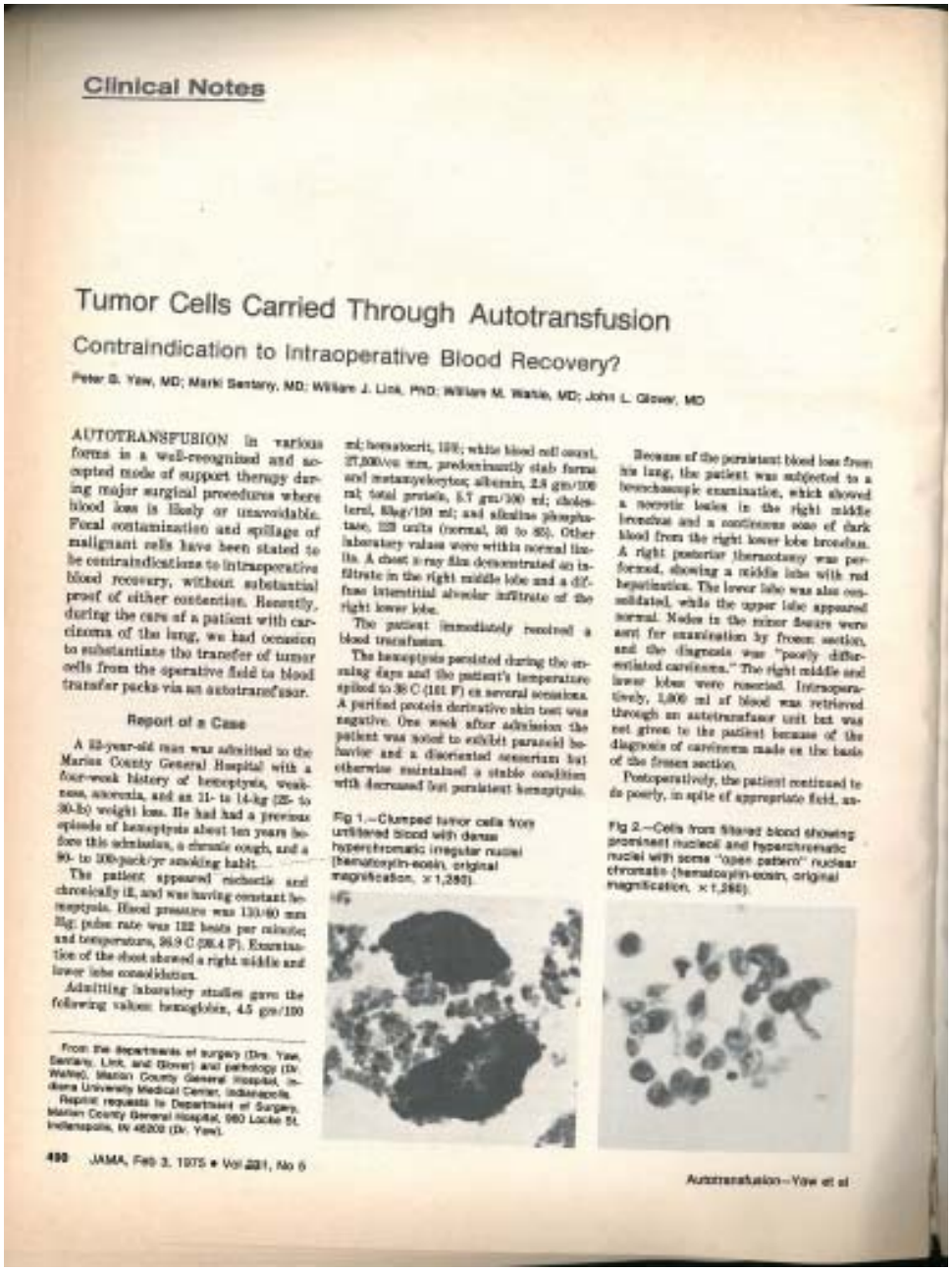
Published:
14 April 2010

Cell salvage for minimising perioperative allogeneic blood transfusion (Review)

Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA

- 75 trials randomizzati;
- Il RIO riduce del 21% il rischio assoluto di ricevere una trasfusione di sangue allogenico (95% CI, 15%-26%);
- L'uso del sangue recuperato comporta un risparmio medio di 0.68 unità di allogenico/paziente (95% CI, 0.49-0.88 unità/paziente);
- …

- ***In chirurgia oncologica il RIO non ha ancora trovato diffusione.***



Clinical Notes

Tumor Cells Carried Through Autotransfusion

Contraindication to Intraoperative Blood Recovery?

Peter B. Yaw, MD; Markl Santory, MD; William J. Link, PhD; William M. Wahle, MD; John L. Glover, MD

AUTOTRANSFUSION in various forms is a well-recognized and accepted mode of support therapy during major surgical procedures where blood loss is likely or unavoidable. Focal contamination and spillage of malignant cells have been stated to be contraindications to intraoperative blood recovery, without substantial proof of either contention. Recently, during the care of a patient with carcinoma of the lung, we had occasion to substantiate the transfer of tumor cells from the operative field to blood transfer packs via an autotransfusor.

Report of a Case

A 53-year-old man was admitted to the Marion County General Hospital with a four-week history of hemoptysis, weakness, anorexia, and an 11- to 14-kg (25- to 30-lb) weight loss. He had had a previous episode of hemoptysis about ten years before this admission, a chronic cough, and a 90- to 100-pack/yr smoking habit.

The patient appeared cachectic and chronically ill, and was having constant hemoptysis. Blood pressure was 130/80 mm Hg; pulse rate was 122 beats per minute; and temperature, 36.9 C (98.4 F). Examination of the chest showed a right middle and lower lobe consolidation.

Admitting laboratory studies gave the following values: hemoglobin, 4.5 gm/100 ml; hematocrit, 13%; white blood cell count, 27,200/cu mm, predominantly stab forms and metamyelocytes; albumin, 2.8 gm/100 ml; total protein, 5.7 gm/100 ml; cholesterol, 83mg/100 ml; and alkaline phosphatase, 128 units (normal, 30 to 85). Other laboratory values were within normal limits. A chest x-ray film demonstrated an infiltrate in the right middle lobe and a diffuse interstitial alveolar infiltrate of the right lower lobe.

The patient immediately received a blood transfusion.

The hemoptysis persisted during the ensuing days and the patient's temperature spiked to 38 C (101 F) on several occasions. A purified protein derivative skin test was negative. One week after admission the patient was noted to exhibit paranoid behavior and a disoriented sensorium but otherwise maintained a stable condition with decreased but persistent hemoptysis.

Because of the persistent blood loss from his lung, the patient was subjected to a bronchoscopic examination, which showed a necrotic lesion in the right middle bronchus and a continuous zone of dark blood from the right lower lobe bronchus. A right posterior thoracotomy was performed, showing a middle lobe with red hepatization. The lower lobe was also consolidated, while the upper lobe appeared normal. Nodes in the minor fissure were sent for examination by frozen section, and the diagnosis was "poorly differentiated carcinoma." The right middle and lower lobes were resected. Intraoperatively, 1,000 ml of blood was retrieved through an autotransfusor unit but was not given to the patient because of the diagnosis of carcinoma made on the basis of the frozen section.

Postoperatively, the patient continued to do poorly, in spite of appropriate fluid, an-

Fig 1.—Clumped tumor cells from unfiltered blood with dense hyperchromatic irregular nuclei (hematoxylin-eosin, original magnification, ×1,280).

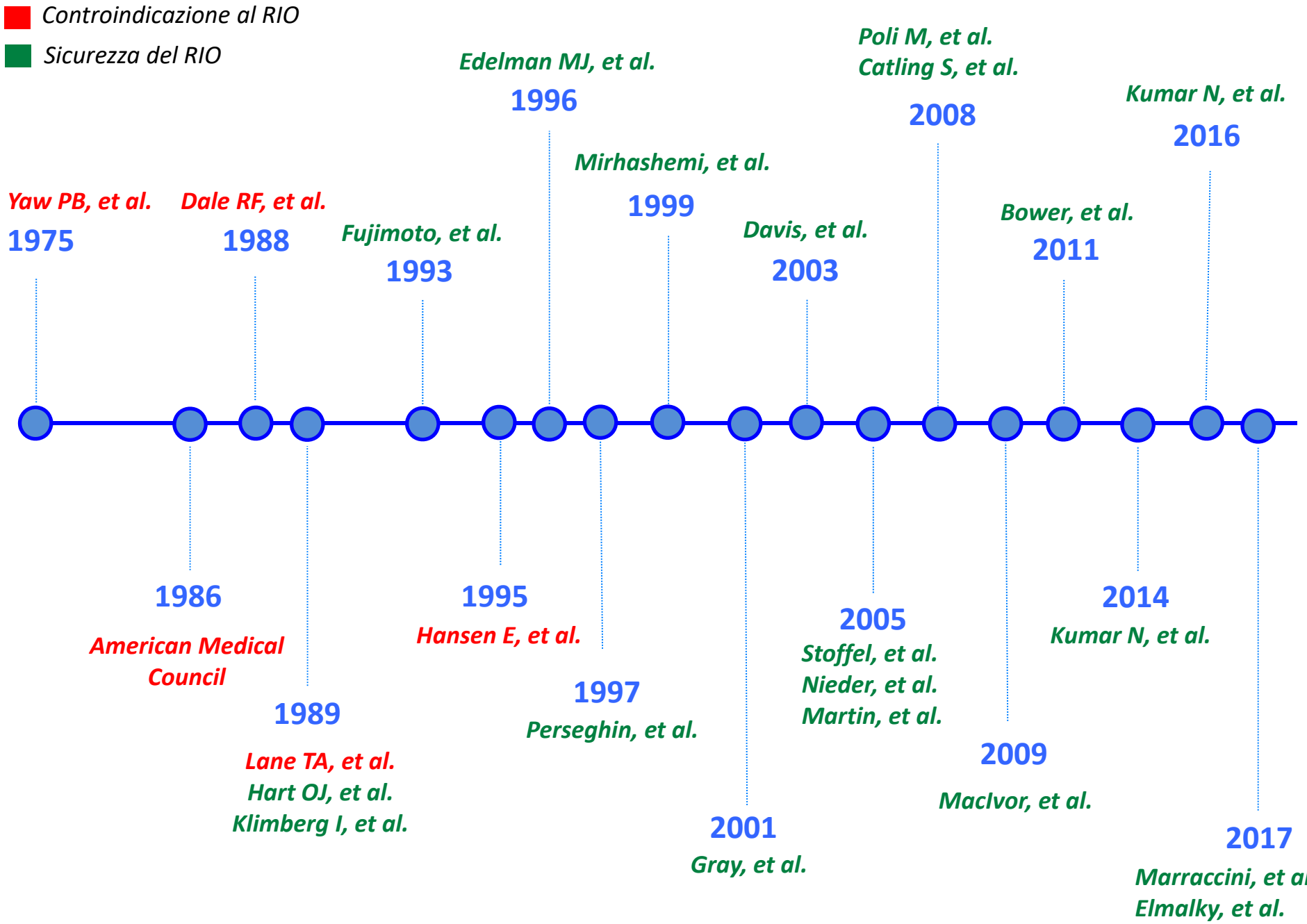
Fig 2.—Cells from filtered blood showing prominent nucleoli and hyperchromatic nuclei with some "open pattern" nuclear chromatin (hematoxylin-eosin, original magnification, ×1,280).

From the Departments of Surgery (Drs. Yaw, Santory, Link, and Glover) and Pathology (Dr. Wahle), Marion County General Hospital, Indiana University Medical Center, Indianapolis. Reprint requests to Department of Surgery, Marion County General Hospital, 960 Locke St, Indianapolis, IN 46202 (Dr. Yaw).

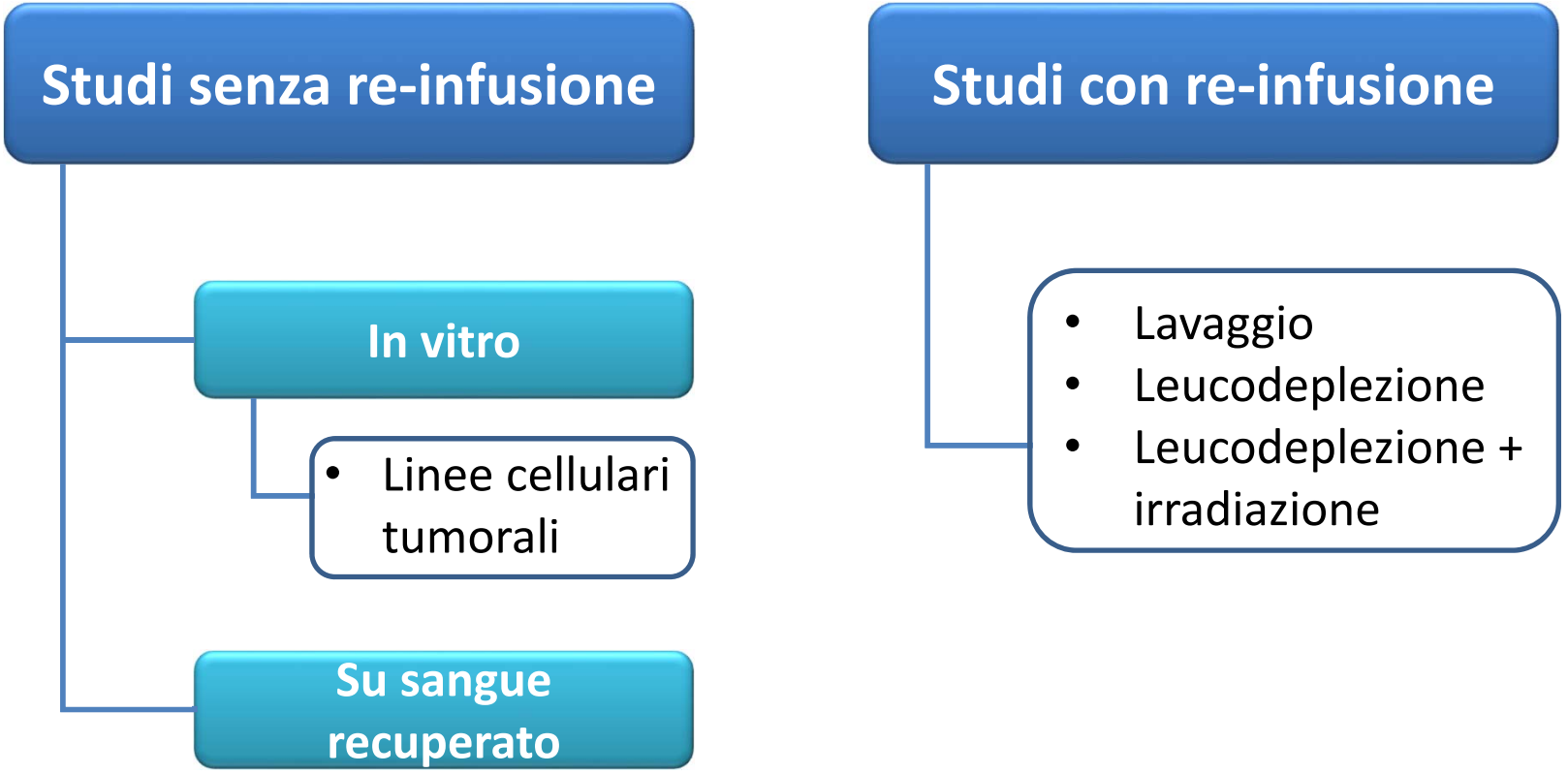
Yaw PB, et al. (1975) JAMA, 231:490-491

«[…]The present case demonstrates that malignant cells are carried through the autotransfusor apparatus. The viability of these passed cells is not known. However, the present evidence seems sufficient to justify the ***warning against the use of an autotransfusor in operations involving resection of malignant tumors, or in those cases where a malignant neoplasm is suspected.****»*

Report on autologous blood transfusion -
American Medical Council (1986):
L'utilizzo del sangue recuperato in chirurgia oncologica è fortemente controindicato.


Controindicazione al RIO
Sicurezza del RIO
Yaw PB, et al.
1975
Dale RF, et al.
1988
Fujimoto, et al.
1993
Edelman MJ, et al.
1996
Mirhashemi, et al.
1999
Davis, et al.
2003
Poli M, et al.
Catling S, et al.
2008
Bower, et al.
2011
Kumar N, et al.
2016
1986
American Medical Council
1989
Lane TA, et al.
Hart OJ, et al.
Klimberg I, et al.
1995
Hansen E, et al.
1997
Perseghin, et al.
2001
Gray, et al.
2005
Stoffel, et al.
Nieder, et al.
Martin, et al.
2009
MacIvor, et al.
2014
Kumar N, et al.
2017
Marraccini, et al.
Elmalky, et al.

Studi sul RIO in chirurgia oncologica



Studi senza re-infusione

Studi senza re-infusione

Short notes

Br. J. Surg. 1988, Vol. 75, June, 581

Separation of malignant cells during autotransfusion

R. F. Dale, R. M. Kipling, M. F. Smith, D. St. J. Collier and P. J. Smith*

*Departments of Surgery and Anaesthesia, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK and *MRC Clinical Oncology and Radiotherapeutics Unit, Medical Research Council Centre, Hills Road, Cambridge, UK*

Correspondence to: Mr D. St. J. Collier

Table 1 *Distribution of labelled tumour cells added to whole blood, before and after processing in the cell saver*

	Experiment 1 SC	Experiment 2 HT29
Before processing		
Whole blood	45650 ± 944	3662 ± 219
RBC fraction	35116 ± 580	3154 ± 149
Sera fraction	8042 ± 836	569 ± 92
After processing and resuspension in normal saline		
Resuspended RBCs	41624 ± 1452	3080 ± 217
RBC fraction	39644 ± 1514	2409 ± 202
Normal saline fraction	1048 ± 86	310 ± 18
Waste (washings)	2448 ± 264	291 ± 14

Values are mean counts per min ± s.e.m.

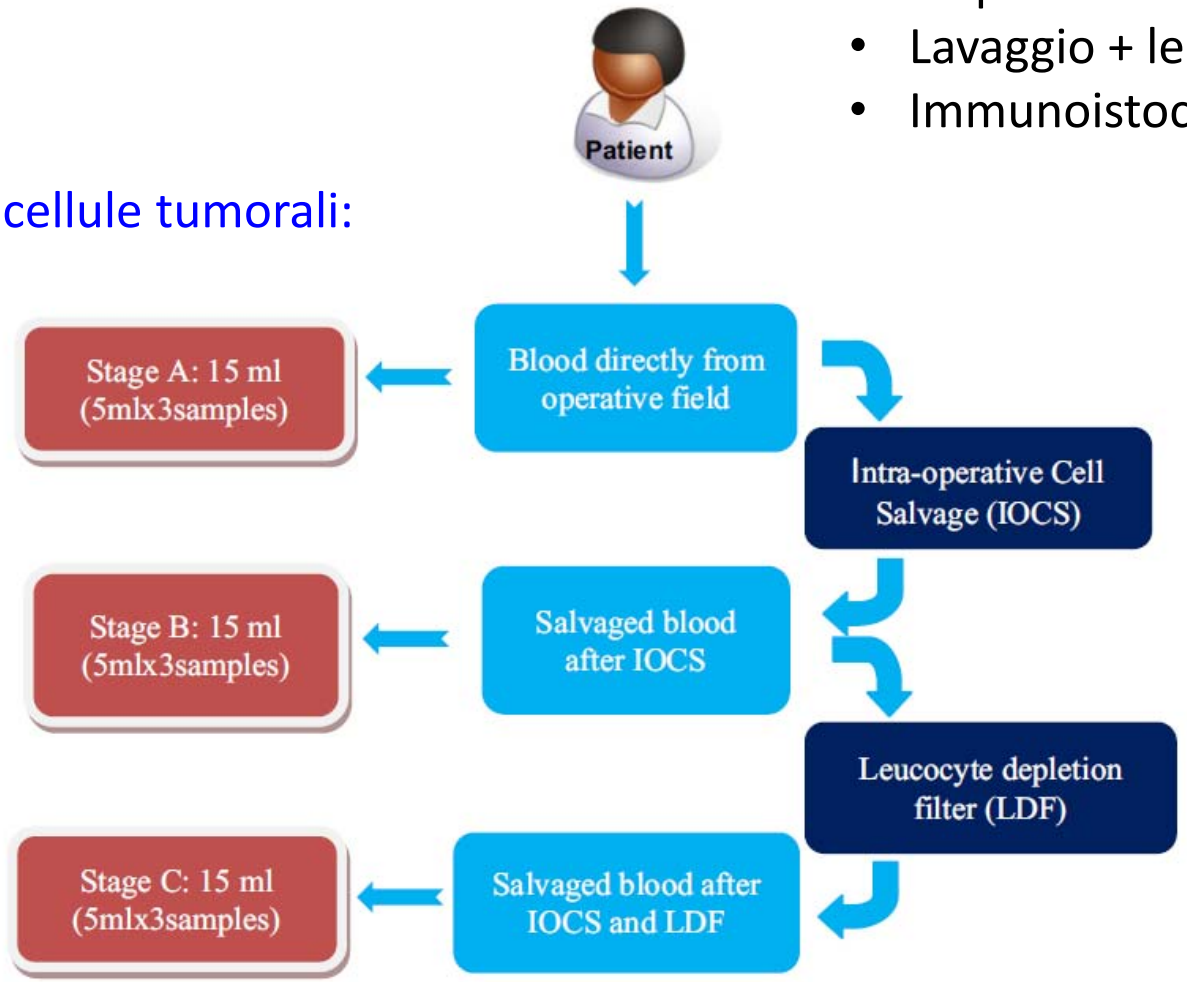
Conclusion: *[…]Tumour cells returned in this way may originate either directly from the tumour at the time of operation or indirectly from the circulation in which they have previously been disseminated.* ***Those using HCS in tumour surgery should be aware that malignant cells may be reinfused into the patient.***

Studi senza re-infusione

Kumar N, et al. ***Are we ready for the use of intraoperative salvaged blood in metastatic spine tumour surgery?*** Eur Spine J.(**2016**), 12:3997-4007.

- 60 pazienti con metastasi spinali
- Lavaggio + leucodeplezione
- Immunoistochimica

Presenza di cellule tumorali:



24/60

4/60

0/60

Studi senza re-infusione

VoxSanguinis
The International Journal of Transfusion Medicine

ISBT International Society of Blood Transfusion

Vox Sanguinis (2017) **112**, 803–805

DOI: 10.1111/vox.12565

SHORT REPORT

Safety of leucodepleted salvaged blood in oncological surgery: an *in vitro* model

C. Marraccini,[1] L. Merolle,[1] P. Berni,[1] K. Boito,[1] I. Tamagnini,[2] E. Kuhn,[2] M. Ragazzi,[2] R. Baricchi[1] & T. A. Pertinhez[1,3]

[1]*Transfusion Medicine Unit, AUSL-IRCCS, Reggio Emilia, Italy*
[2]*Pathological Anatomy Unit, AUSL-IRCCS, Reggio Emilia, Italy*
[3]*Department of Medicine and Surgery, University of Parma, Parma, Italy*

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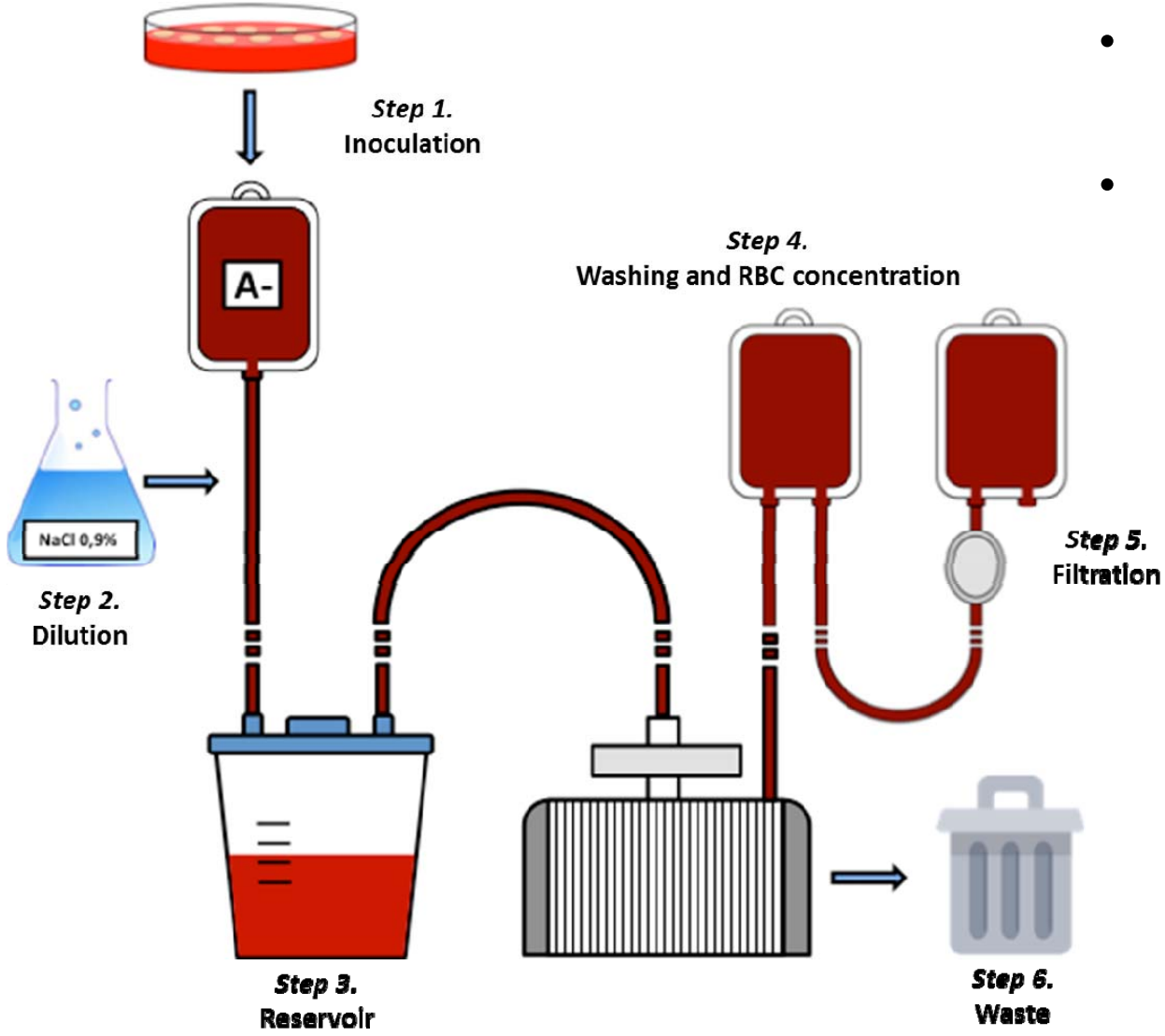
Schema dell'esperimento

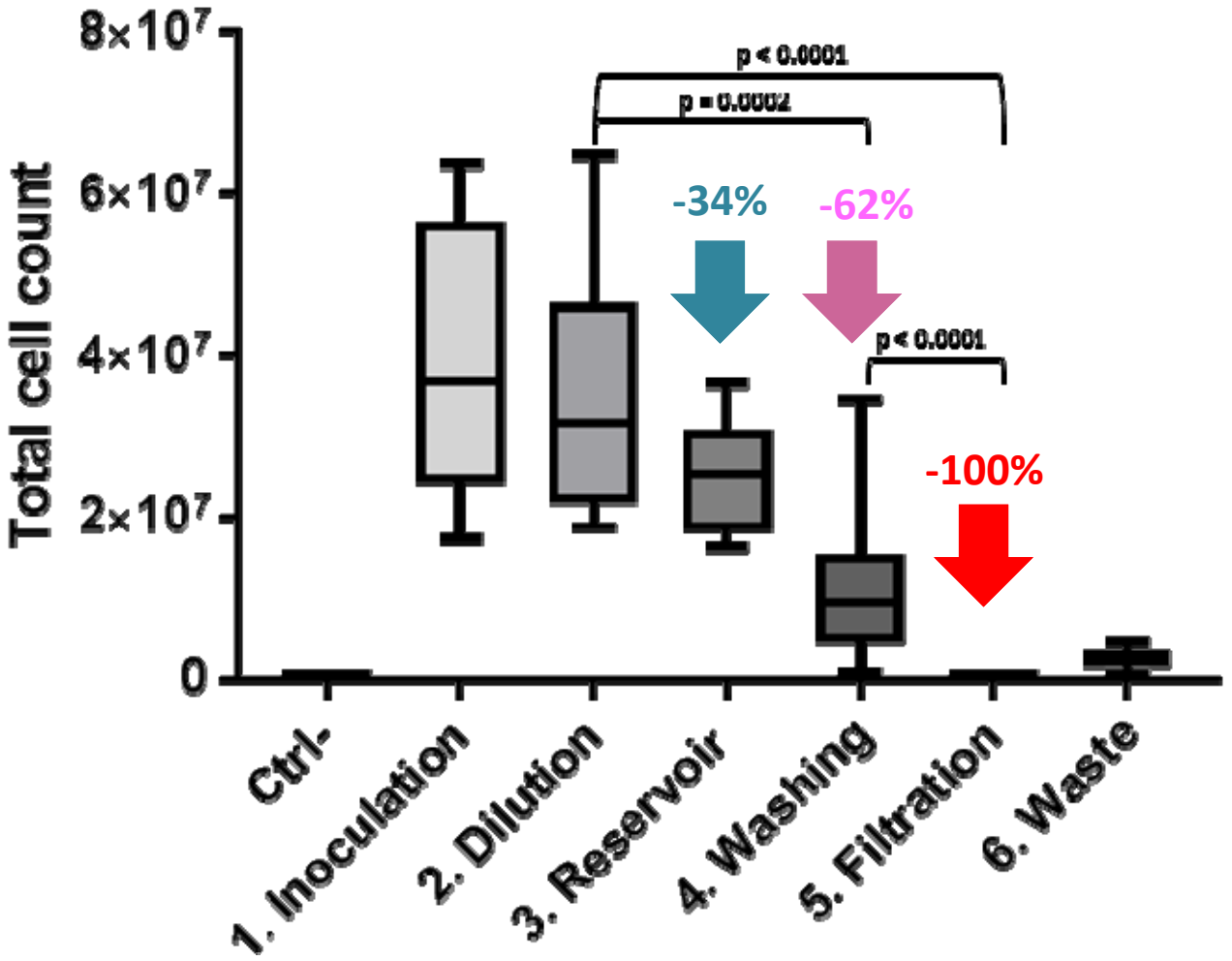
HCT116 (Human Colorectal Cancer cell line)



Analisi:

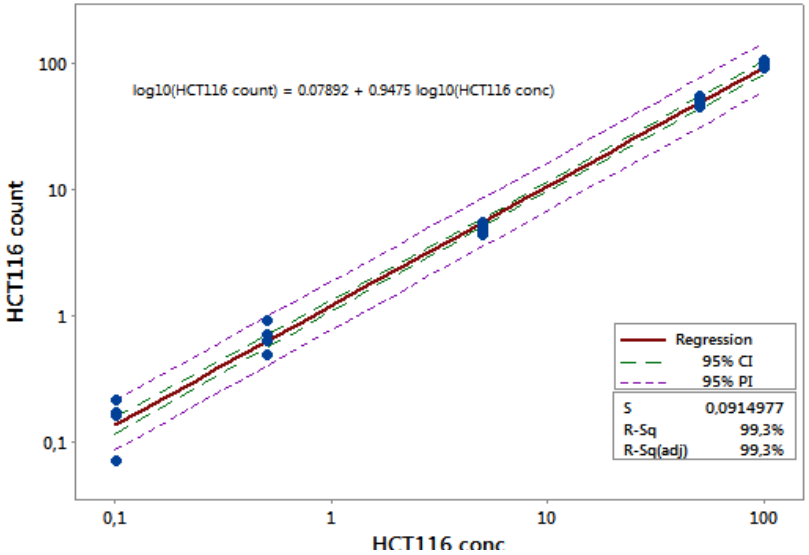
- Citofluorimetria (CD45/CD326-EpCAM)
- Immunoistochimica

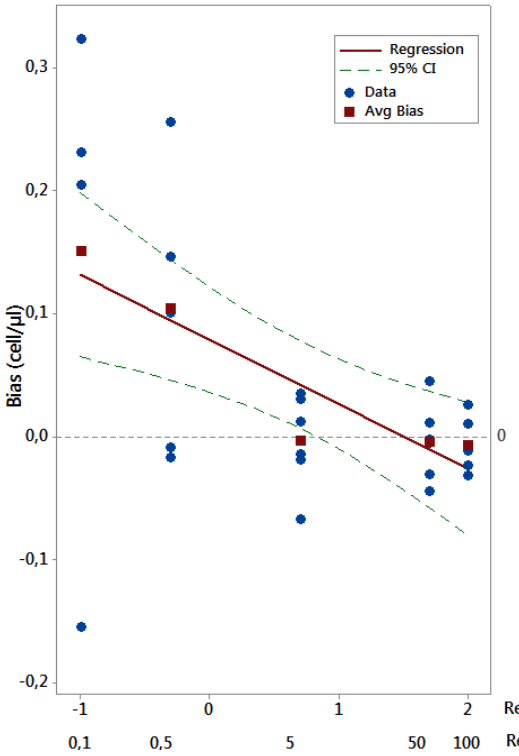
Conta delle cellule HCT116 residue nel sangue recuperato e filtrato:



Gage linearity and bias study

The blood samples were inoculated with a fixed amount of HCT116 cells at the concentrations of 0.1-0.5-1-5-10-50-100 cells/mL.
The quantitative assessment of HCT116 cells was performed with flow cytometry using anti-CD326-PE monoclonal antibody.
Using Minitab software, a study of least squares regression was performed (R^2 99.3%). It was necessary to apply a logarithmic transformation on collected data in order to satisfy the homogeneity of variances assumption for the errors and to linearize the fit. For each concentration, we randomly collected 6 repeated measures.





Gage Linearity

Predictor	Coef	SE Coef	P
Constant	0,07892	0,02082	0,001
Slope	-0,05248	0,01577	0,003

S 0,0914977 R-Sq 29,9%

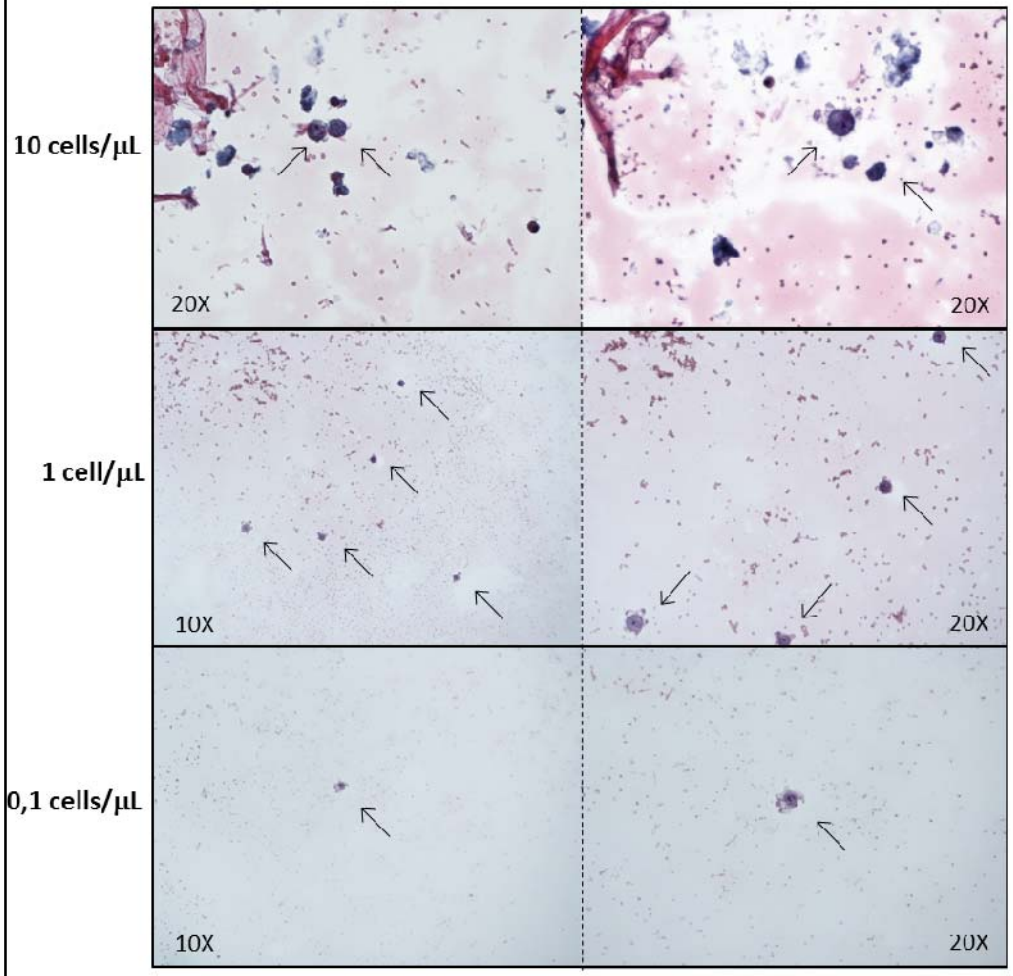
Gage Bias

Reference	Bias	P
Average	0,040343	0,032
-1	0,150472	0,247
-0,301030	0,103566	0,059
0,698970	-0,003996	0,808
1,69897	-0,004725	0,729
2	-0,006891	0,460

L’analisi citofluorimetrica ci consente di rilevare con precisione fino a 0,2 cellule/µL.

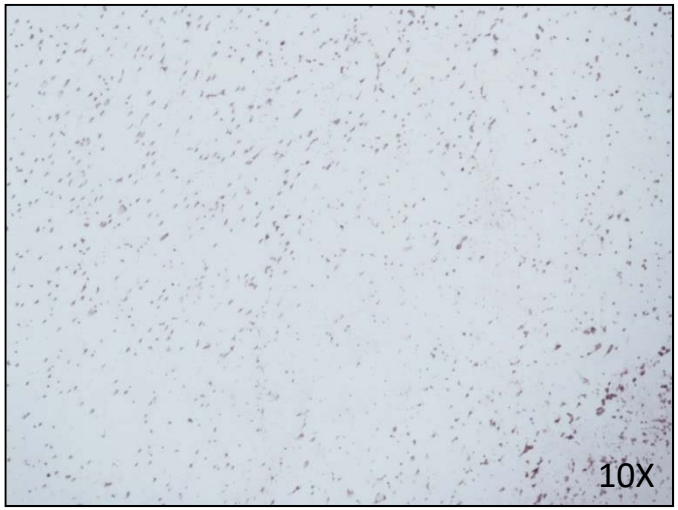
Test di Papanicolau

Vetrini di emazie «contaminate» con quantità note di cellule tumorali HCT116:



Emazie «contaminate» con HCT116 (150 cells/µL), sottoposte a lavaggio e leucodeplezione :

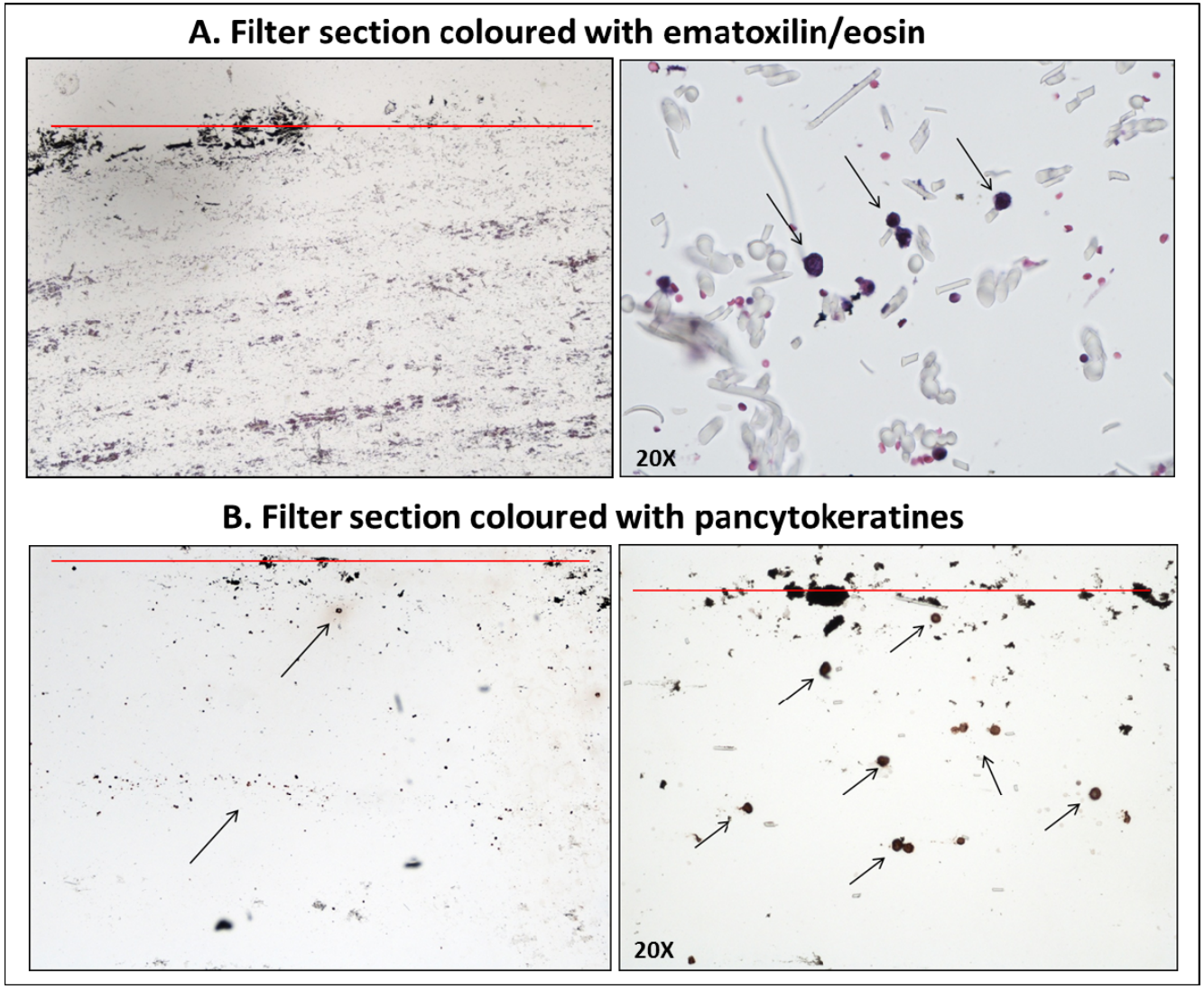
***Step 5.* Filtrato**



La quantità di cellule tumorali residue dopo lavaggio e leucodeplezione è inferiore a 0,1 cells/µL.

Sezione del filtro per leucodeplezione

Le cellule tumorali sono trattenute dai primi 2 (di 20) strati del filtro per leucodeplezione:



Studi con re-infusione

Analysis of peripheral blood for prostate cells after autologous transfusion given during radical prostatectomy

JOHN T. STOFFEL, LINDA TOPJIAN and JOHN A. LIBERTINO
Department of Urology, Lahey Clinic, Burlington, MA, USA

Accepted for publication 29 March 2005

OBJECTIVES

To determine if cells expressing prostate-specific antigen (PSA) can be detected in blood collected by a cell-saver during radical prostatectomy (RP) or in the peripheral blood after intraoperative autotransfusion (IAT).

PATIENTS AND METHODS

In all, 112 men with clinical T1c–T2 prostate cancer undergoing RP were prospectively assessed. A cell-saver system was used in each to collect blood from the surgical field after prostate manipulation. IAT was given based on clinical indications. Standardized peripheral blood samples were collected from patients before RP, in the recovery room afterward, and at 3–5 weeks after surgery. A reverse-transcriptase-polymerase chain reaction assay for PSA mRNA was used to detect prostate cells in cell-saver and peripheral blood samples. Patients were followed after surgery with PSA measurements to assess biochemical failure.

RESULTS

PSA-expressing cells were detected in 88% of cell-saver reservoir and 13% of preoperative blood samples. No PSA-expressing prostate cells were detected in any peripheral blood samples collected 3–5 weeks after surgery. Analysis of data with 40 months of follow-up showed IAT was not an independent predictor of biochemical failure in multivariate analysis.

CONCLUSIONS

Although IAT blood contains PSA-expressing cells, none could be detected 3–5 weeks after surgery. IAT during RP was not associated with a greater risk of biochemical failure.

KEYWORDS

prostate cancer, surgery, transfusion, PSA, cells

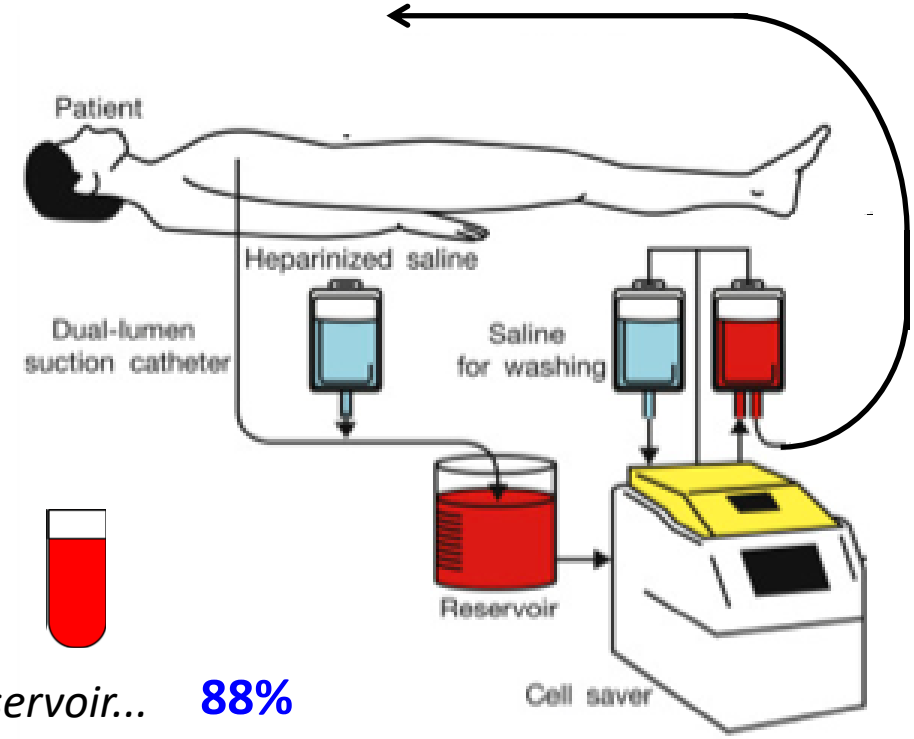
Studi di re-infusione su pazienti

Stoffel JT, et al. **Analysis of peripheral blood for prostate cells after autologous transfusion given during radical prostatectomy.** BJU Int. (**2005**), 96(3):313-5.

- 112 pazienti sottoposti a prostatectomia radicale
- Presenza di PSA mediante RT-PCR

prima dell'intervento...

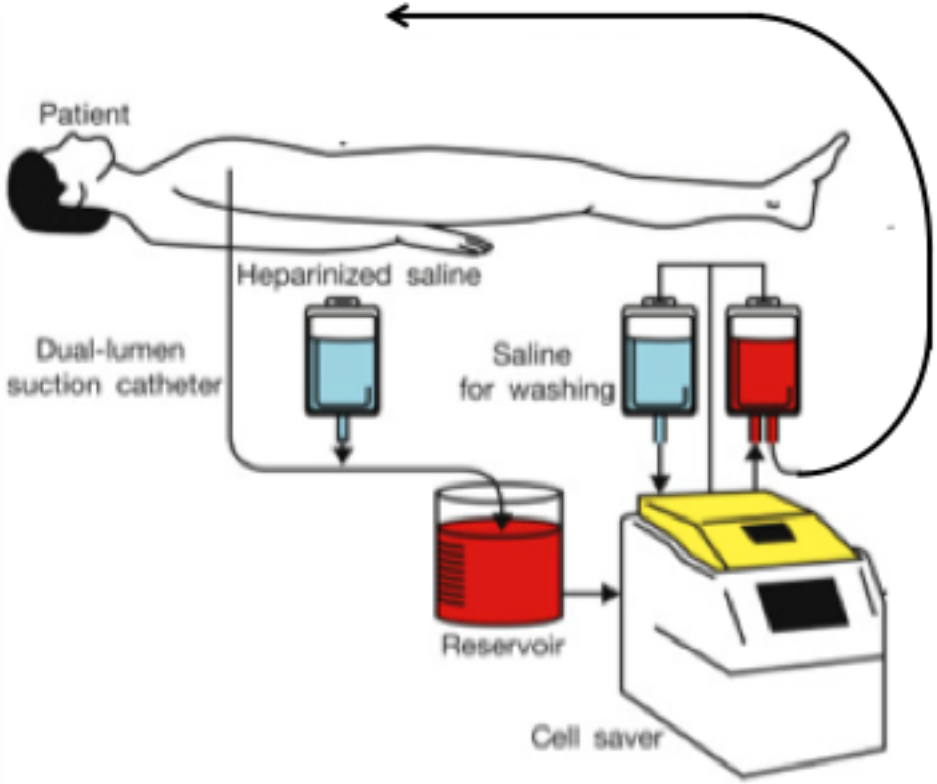
13%



...nel reservoir... **88%**

...dopo 5 settimane

0%


Patient
Heparinized saline
Dual-lumen
suction catheter
Saline
for washing
Reservoir
Cell saver

Studi di re-infusione su pazienti

Nieder AM, et al. **Intraoperative cell salvage during radical prostatectomy is not associated with greater biochemical recurrence rate**. Urology (2005), 65(4):730-734.

- 1038 pazienti con carcinoma della prostata tra il 1992 e il 2003
- 265 hanno ricevuto sangue recuperato e 773 no

- 3% RIO allotrasfusi
- 14% non-RIO allotrasfusi

Rischio di *biochemical recurrence* a 5 anni simile tra i due gruppi:

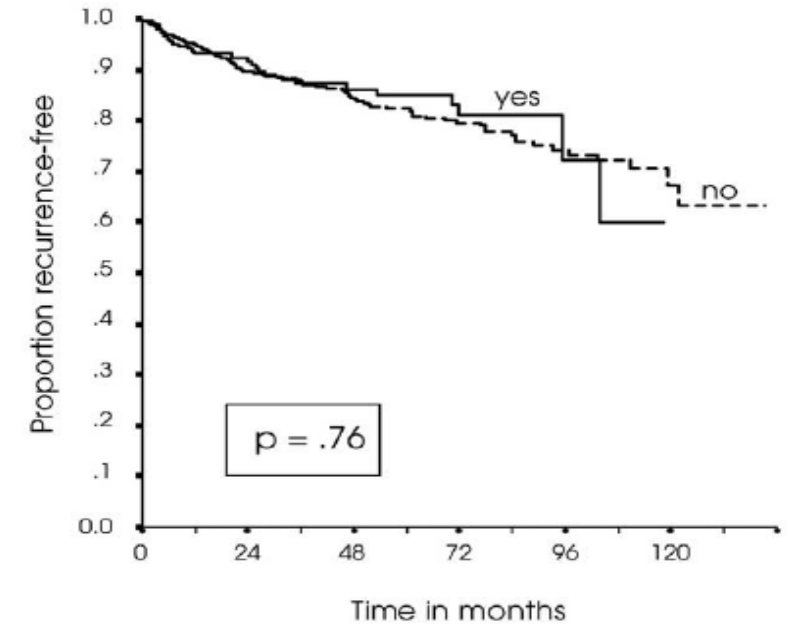
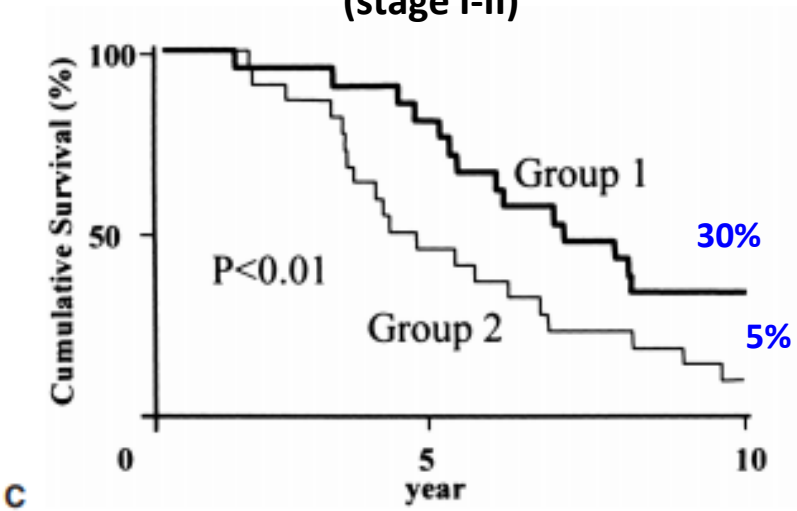


FIGURE 1. *Kaplan-Meier curve comparing PSA recurrence for all patients.*

Studi di re-infusione su pazienti

Hirano T et al. ***Long-Term Safety of Autotransfusion During Hepatectomy for Hepatocellular Carcinoma.*** Surgery Today (**2005**), 35:1042–1046.

Early-stage Hepatocarcinoma (stage I-II)



Stage III-IV Hepatocarcinoma

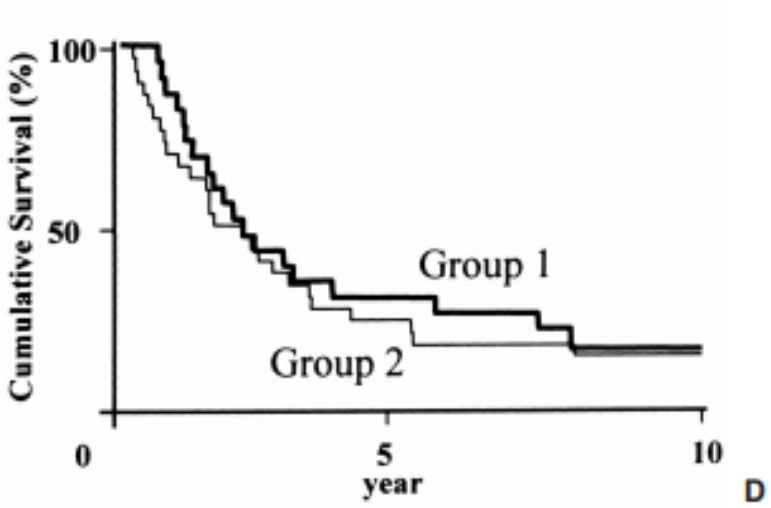


Table 1. Comparison of distal metastasis after hepatectomy with and without homologous blood transfusion

	No. of patients	
	Group 1	Group 2
Brain		1
Lung	7	6
Bone	3	7
Adrenal gland	1	1
Skin	1	1
Total	12	16

Group 1 (IOCS)		Group 2 (control)	
Total	Allo-transfused	Total	Allo-transfused
46	31 (67%)	50	49 (98%)

Waters JH et al. **Blood salvage and cancer surgery: a meta-analysis of available studies.** Transfusion (**2012**) 52:2167-2173.

Study	Nation	Cancer	Study design	Control group	IOCS		Control		
					Total	allo-transfused intra-op	Total	allo-transfused intra-op	
Fujimoto et al., 1993	Japan	Hepatocarcinoma	historical case control	allogenic transfusion	54	814 mL mean	50	3466 mL mean	
Connor et al., 1995	U.S.A.	Cervical cancer	prospective cohort, historical case control	not reinfused	31	1	40	4	* **Reduced intra-/post-op allo-transfusion**
Mirhashemi et al., 1999	U.S.A.	Cervical cancer	retrospective cohort	allogenic transfusion	50	6 (12%)	106	32 (30%)	*
Gray et al., 2001	U.S.A.	Prostate cancer	historical case control	preoperative autologous donation	62	2 (3%)	101	14 (14%)	* **Use of LDF**
Davis et al., 2003	Israel	Prostate cancer	retrospective cohort	preoperative autologous donation, allogenic transfusion	87	0	321	0	
Muscari et al., 2005	France	Hepatocarcinoma	prospective cohort	not reinfused	31	0	16	0	
Stoffel et al., 2005	U.S.A.	Prostate cancer	prospective cohort	not reinfused	48	0	64	0	
Nieder et al., 2005	U.S.A.	Prostate cancer	retrospective cohort	allogenic transfusion	265	4 (1,5%)	773	5 (0,7%)	
Hirano et al., 2005	Japan	Hepatocarcinoma	historical case control	allogenic transfusion	46	31 (67%)	50	49 (98%)	*
MacIvor et al., 2009	U.S.A.	Prostate cancer	retrospective cohort	preoperative autologous donation	63	2	40	0	
Bower et al., 2011	U.S.A.	Gastrointestinal cancer	prospective cohort	not reinfused	32	0	60	0	

Studi di re-infusione su pazienti

Waters JH et al. **Blood salvage and cancer surgery: a meta-analysis of available studies.** Transfusion (**2012**) 52:2167-2173.

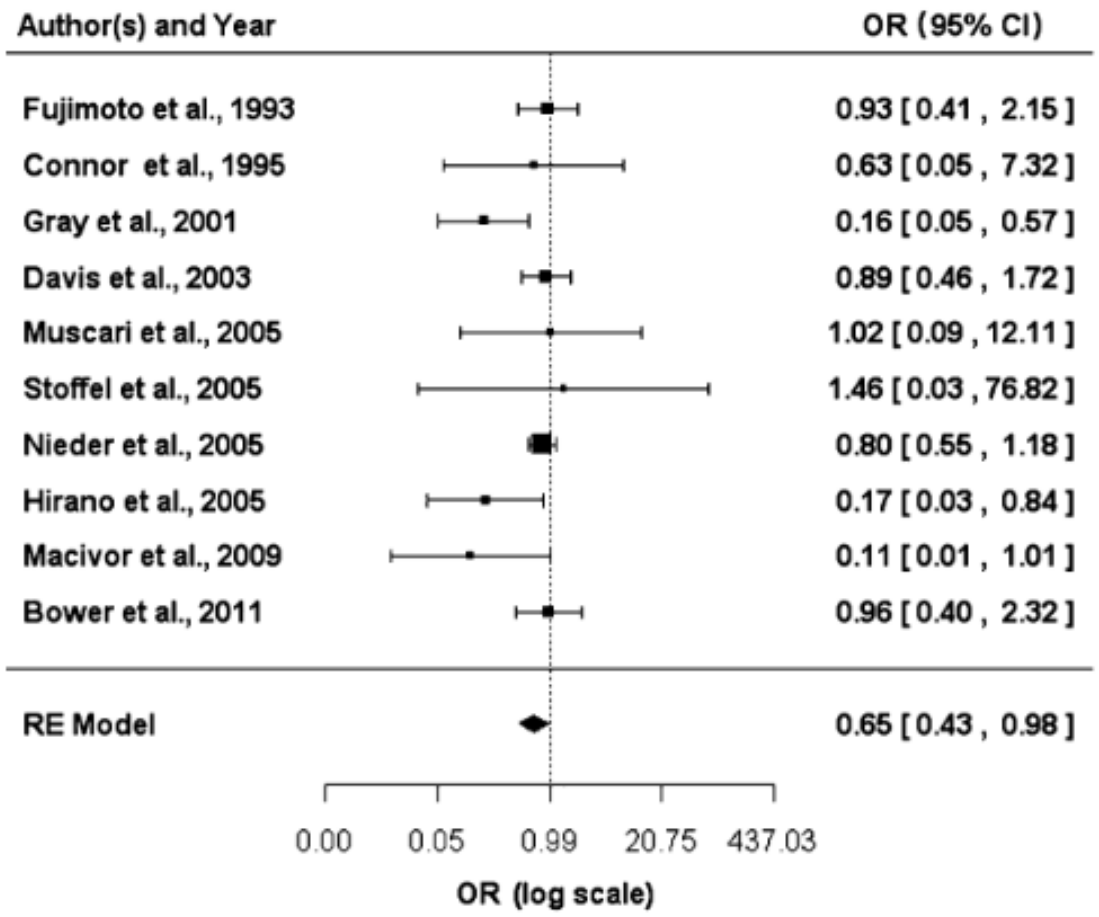


Fig. 1. Forest plot for all studies of cancer recurrence after IBS use versus control. Values less than 1 favor the group of patients who received IBS during their cancer surgeries.

- 10 studi
- 741 pazienti che hanno ricevuto sangue da RIO
- 1585 pazienti controllo
- 1/10 con leucodeplezione
- 0/10 con irradiazione

- *Non inferiorità del RIO rispetto alla trasfusione allogenica;*
- *Significativa riduzione delle trasfusioni allogeniche nei gruppi RIO.*

Studi di re-infusione su pazienti

Elmalky M et al. **The safety, efficacy, and cost-effectiveness of intraoperative cell salvage in metastatic spine tumor surgery.** The Spine Journal (**2017**), 977-982.

Variable	RIO+LDF Cases (n=63)	non - RIO Controls (n=113)	All patients (n=176)
Gender			
Male (frequency [valid %])	45 (71.4%)	61 (54.0%)	106 (60.2%)
Female (frequency [valid %])	18 (28.6%)	52 (46.0%)	70 (39.8%)
Length of stay in days (mean [SD])	15.9 (7.38)	19.1 (9.96)	17.9 (9.19)
Preoperative anemia			
No anemia (frequency [valid %])	29 (46.0%)	58 (51.3%)	87 (49.4%)
Anemia (frequency [valid %])	34 (53.0%)	55 (48.7%)	89 (50.6%)
Surgical complications			
No complications (frequency [valid %])	59 (95.2%)	107 (99.1%)	166 (97.6%)
Complications (frequency [valid %])	3 (4.8%)	1 (0.9%)	4 (2.4%)
Patient survival			
Death recorded (frequency [valid %])	26 (41.3%)	51 (45.1%)	77 (43.8%)
No death recorded (frequency [valid %])	37 (58.7%)	62 (54.9%)	99 (56.2%)
Procedural cost (mean [SD])	GBP351.78 (GBP207.21)	GBP338.42 (GBP314.85)	GBP340.77 (GBP286.67)

- RIO+LDF è significativamente associato a riduzione trasfusioni allogeniche
- RIO+LDF non è associato a aumento dei costi
- RIO+LDF è associato a degenza media più breve
- Sopravvivenza a 5 anni e complicanze comparabili tra i due gruppi

Come dimostrare che il RIO oncologico è sicuro?

Evidenze cellulari di base

- Verifica della presenza di CTCs nel sangue recuperato

Evidenze cellulari avanzate

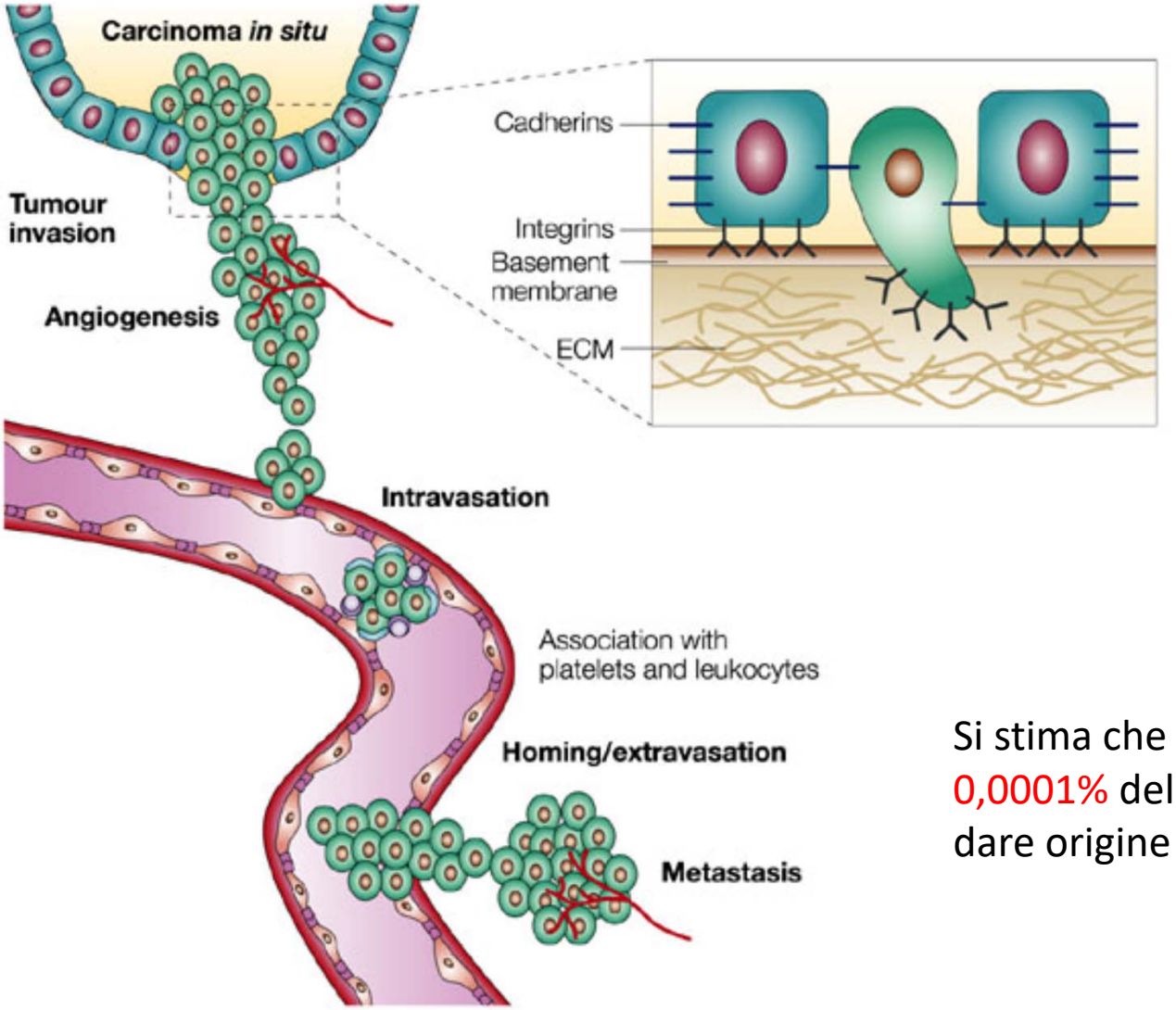
- Quantificazione delle CTCs nel sangue recuperato e confronto con il sangue periferico del paziente

Evidenze cliniche

- Stabilire l'effetto della re-infusione di sangue recuperato sugli outcomes (OS, PFS, recidive,…)

E' necessario un trial clinico prospettico randomizzato!

CTCs e metastasi…



Si stima che solo tra lo 0,01% e lo 0,0001% delle CTCs sia in grado di dare origine a metastasi.

(*Chambers et al., 2002*)

La trasfusione allogenica è importante, ma…

- La maggioranza delle trasfusioni di emazie è a scopo profilattico
- La trasfusione allogenica è un fattore di rischio indipendente per esiti clinici sfavorevoli
- La trasfusione di emazie in pazienti emodinamicamente stabili è una causa di patologie iatrogene

Nei pazienti oncologici…

- Impatto negativo su sopravvivenza nel post-operatorio
- Significativamente associato a minor tempo di recidiva
- Numero di unità trasfuse direttamente correlato con il peggioramento degli outcomes

Cosa dicono le linee guida nel mondo…

<u>Non esistono</u> controindicazioni assolute all'utilizzo del recupero intraoperatorio in chirurgia oncologica.

General indications for cell salvage (AABB)

Specialty	Surgical procedure	Comments
Cardiac	Valve replacement Redo bypass grafting	
Orthopaedics	Major spine surgery Bilateral knee replacement Revision of hip replacement	
Urology	Radical retropubic prostatectomy Cystectomy Nephrectomy	Individualised by surgeon Limited to patients with prior radiation therapy When tumour involves major vessels
Neurosurgery	Giant basilar aneurysm	
Vascular	Thoraco-abdominal aortic aneurysm repair Abdominal aortic aneurysm repair	Should be individualised by surgeon and patient's characteristics
Liver Transplant		
Other	Jehovah's Witnesses Unexpected massive blood loss Red cell antibodies	When accepted by patient

NICE

Indications

Intraoperative red blood cell salvage may be required during prostatectomy and radical cystectomy operations to treat malignancy. Despite improvements in techniques considerable blood loss may occur.

Cosa dicono le linee guida…

Cosa dicono le EDQM…

Haemorrhage in cancer patients: although the passing of blood through a leucodepletion filter significantly reduces the number of retransfused tumour cells, the salvaged cells should be irradiated.

Obstetric haemorrhage: use of leucodepletion filters in obstetric haemorrhage provides a significant reduction in contamination of cells from amniotic fluid. This is also true for caesarean section. There is also concern regarding reinfusion of foetal red cells from the operative field. If the mother is RhD-negative and the foetus RhD-positive, the extent of maternal exposure should be determined as soon as possible, and a suitable dose of human anti-D immunoglobulin should be administered.

EDQM
19th Edition
2017

…cosa dice la SIMTI

Chirurgia oncologica

Diversi studi prospettici e retrospettivi dimostrano che il RIO può essere impiegato allo scopo di ridurre il ricorso alla trasfusione allogenica, senza aumentare il rischio di recidiva, negli interventi di chirurgia oncologica in urologia (prostatectomia radicale, cistectomia radicale)[236-243], ginecologia[244], negli interventi di resezione[245] o di trapianto epatico[246], in interventi di chirurgia toracica[247] e in interventi combinati di chirurgia oncologica e cardiovascolare[248].

Un'elevata percentuale di questi pazienti ha cellule tumorali in circolo, senza che questo sia stato correlato ad una riduzione della sopravvivenza dopo l'intervento chirurgico[154,249]; infatti solo una limitata percentuale di queste cellule ha capacità di metastatizzare (da $1/10^4$ a $1/10^8$)[154,250].

I filtri da leucodeplezione sono stati impiegati per ridurre il numero delle cellule tumorali presenti nel sangue recuperato durante gli interventi di chirurgia oncologica[154,243,244,246,247,251-253]. La filtrazione è stata abbinata con successo all'irradiazione dei CE ottenuti da RIO[16,251,253-257].

In chirurgia oncologica, nell'ambito di protocolli locali che tengano conto delle caratteristiche del singolo paziente (rischio emorragico, alloimmunizzazione multipla) e dell'esperienza del *team* chirurgico e anestesiologico, si suggerisce l'adozione del RIO, purché la trasfusione delle EC recuperate avvenga mediante filtri da leucodeplezione e sia preceduta da irradiazione (25 Gy) delle stesse (*Grado di raccomandazione: 2C*)[16,27,154,236-257].

Raccomandazioni SIMTI sulla trasfusione perioperatoria

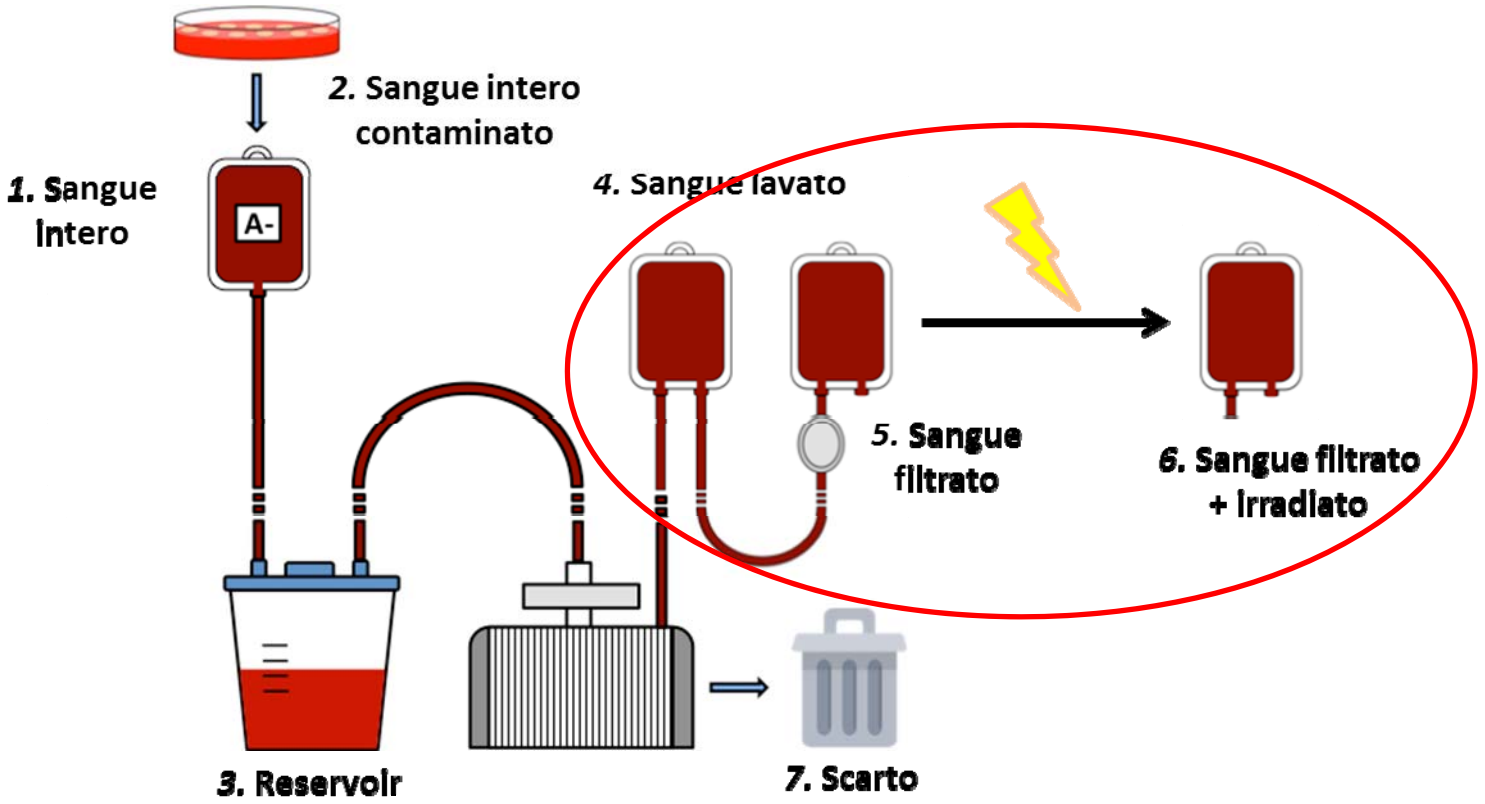
1ª Edizione
Giugno 2010

Prospettive future…a Reggio Emilia

Piano Sangue e Plasma 2017-2019.
Finanziamenti per l'attivazione di nuovi progetti in ambito trasfusionale per il biennio 2018-2019: **Progetti Patient Blood Management (PBM) - D. lgs 207/2007**

"Recupero intraoperatorio in chirurgia oncologica complessa: quale sangue?"

Prospettive future…a Reggio Emilia



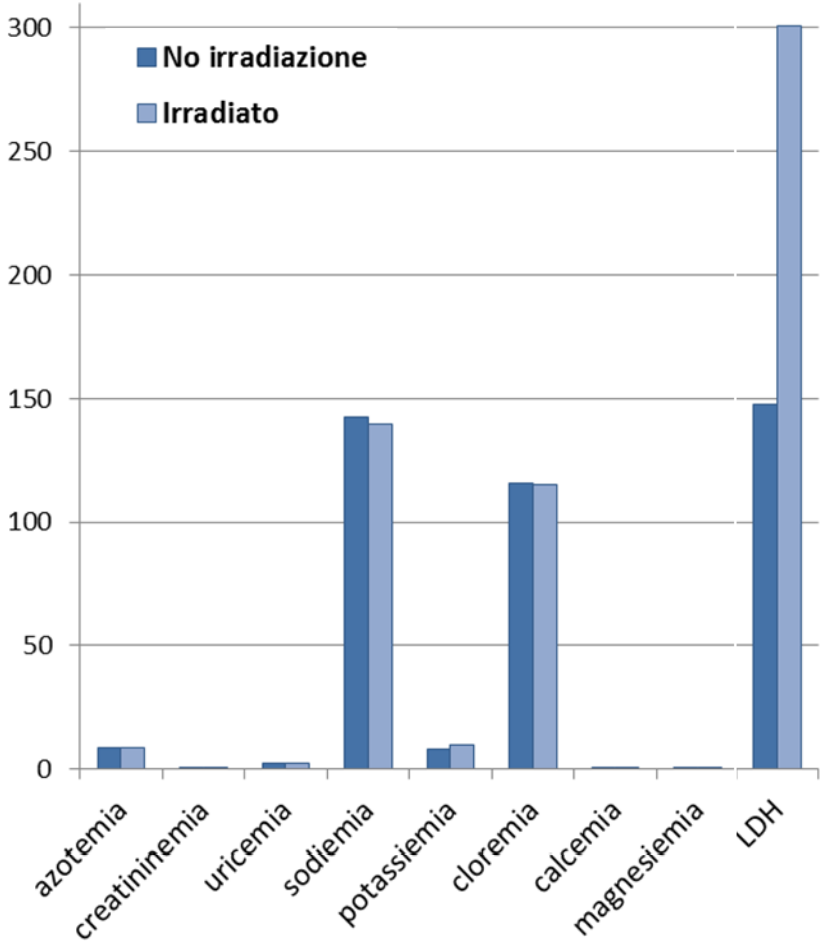
Aspetti qualitativi del sangue recuperato:

- Qualità dei globuli rossi;
- LDH, ammonemia , elettroliti;
- Profilo metabolico

Effetto dell'irradiazione sulle emazie concentrate

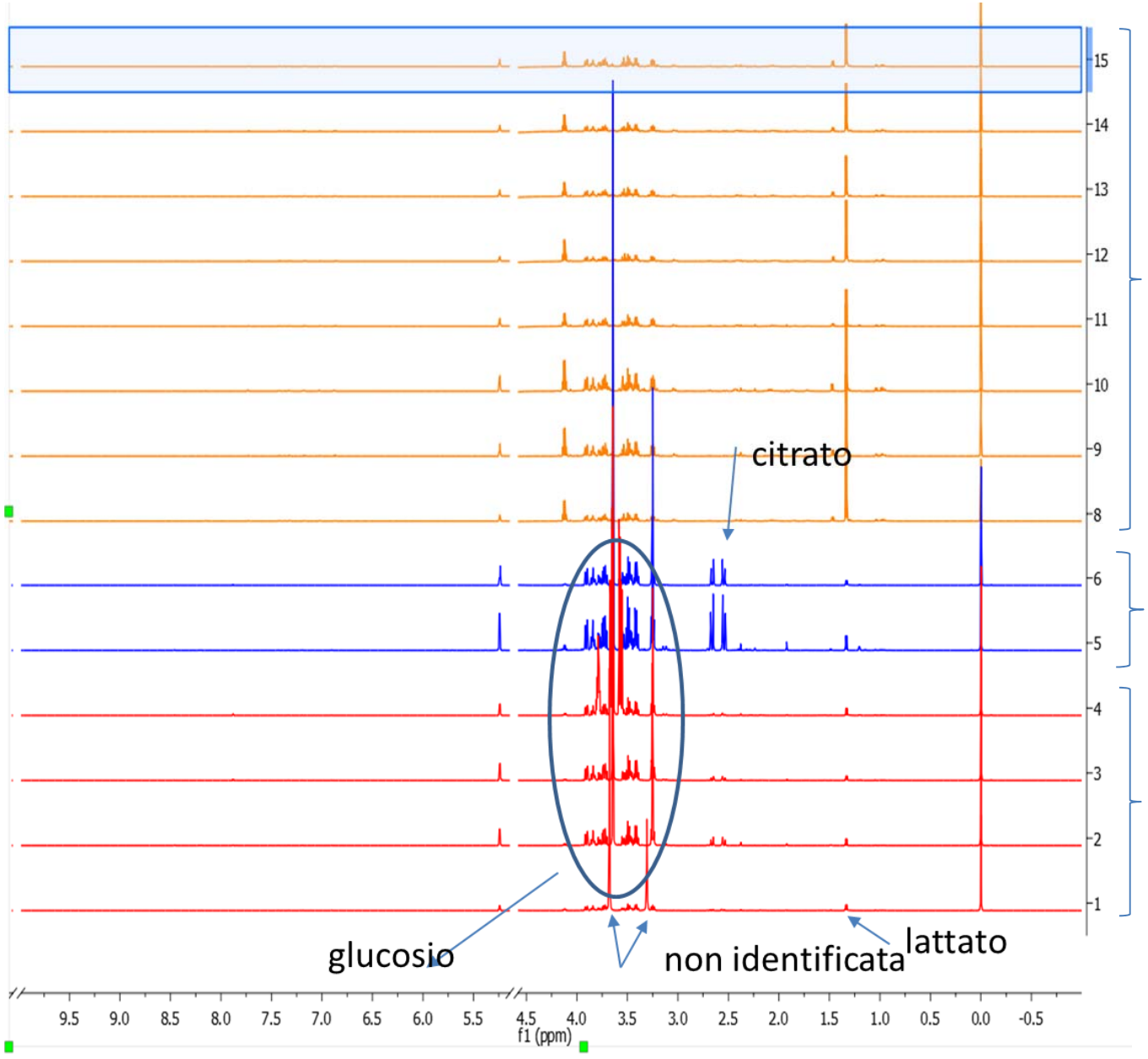
% WBC residui vitali	
Leucodepleti	**Irradiati**
94,6 ± 4,7	96,1 ±3,6

Ammonemia (μg/dL)	
Leucodepleto	**Irradiato**
399 ± 35	432 ± 48



From: F. Baroni et al. **Red blood cells metabolome changes upon treatment with different X-ray irradiation doses.** Annals of Hematology (2018) 97:1909–1917.

Analisi metabolomica con ^{1}H-NMR

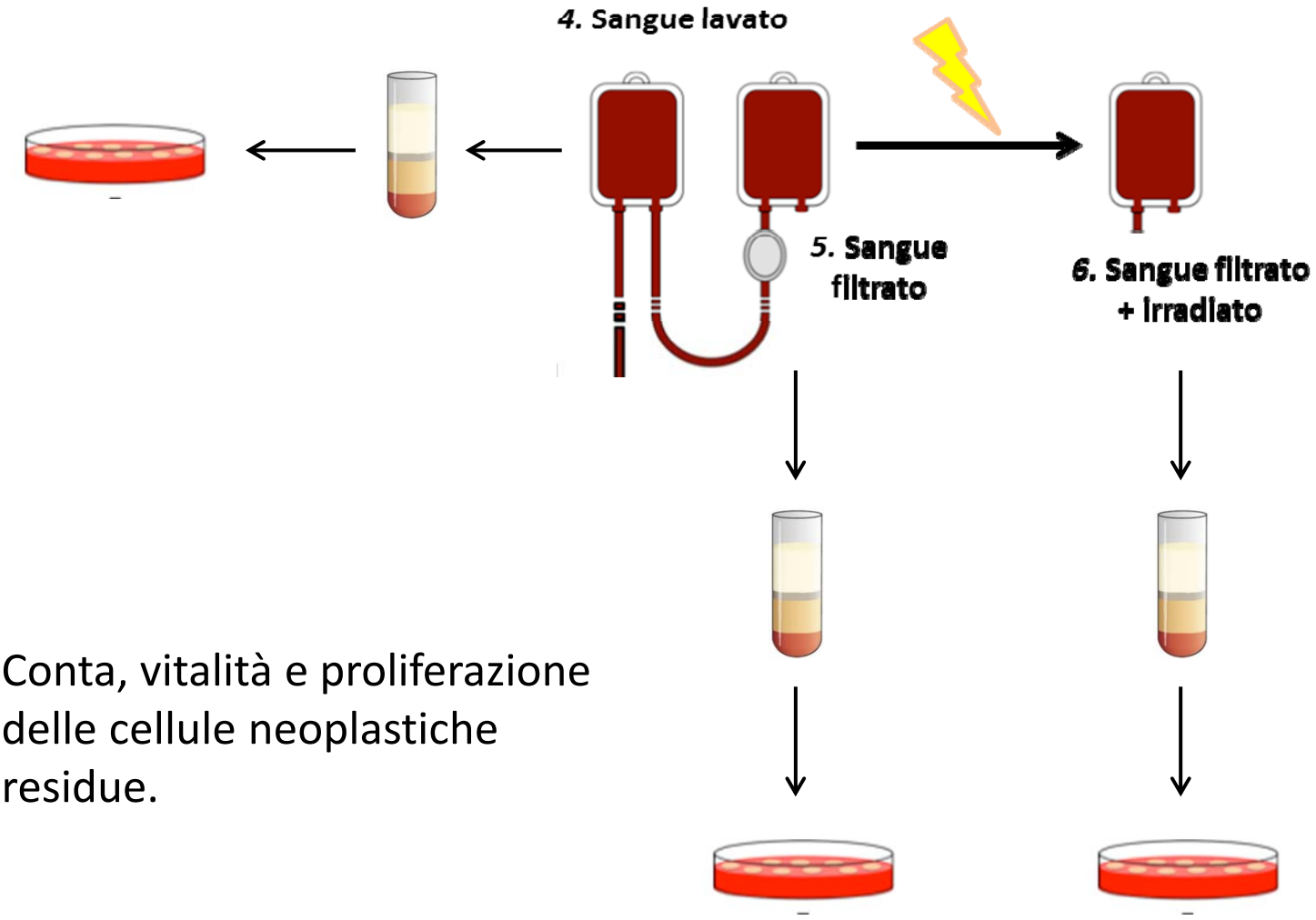


Siero da sangue periferico

Siero da RIO in chirurgia vascolare

Siero da RIO in chirurgia ortopedica

Prospettive future…a Reggio Emilia



- Conta, vitalità e proliferazione delle cellule neoplastiche residue.

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OECI CLINICAL Cancer Centre

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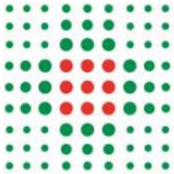
Sala Malatesta Novello
28 - 29 Marzo 2019

Laboratorio di Metabolomica

S.C. Medicina Trasfusionale



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Dr. Roberto Baricchi (Direttore)
Prof.ssa Thelma Pertinhez (UNIPR)

Chiara Marraccini, PhD
Lucia Merolle, PhD
Eleonora Quartieri
Clara Indira Dadomo, MD
Erminia Di Bartolomeo, MD

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