参考資料3（マコファルマ社）

SAFETY OF BLOOD PRODUCTS

THERAFLEX MB Plasma

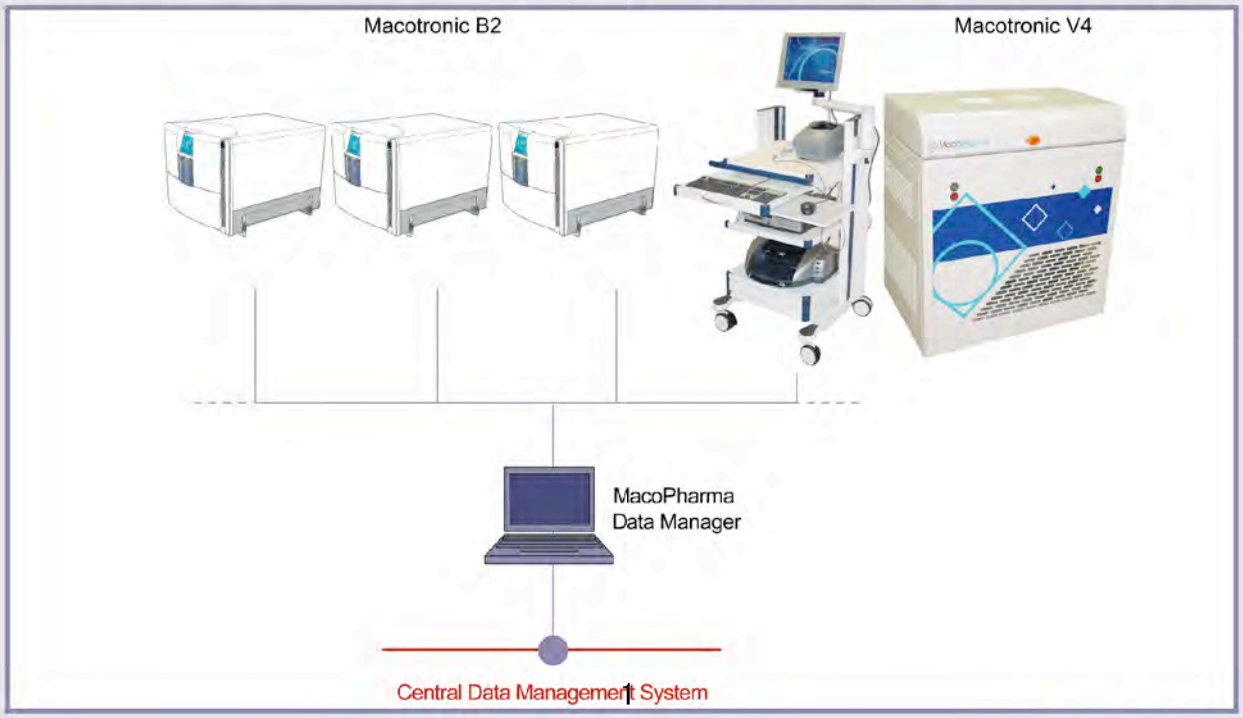
PATHOGEN INACTIVATION SYSTEM FOR PLASMA

Contributing to 10 years of safer Pathogen Inactivated Plasma

- Routine use worlwide: over 4 million MB Plasma units transfused
- Proven clinical efficacy
- In-house processing
- User friendly technology

New Developments:
Macotronic B2, next generation of illumination equipment

- New light source: LED (Light-Emitting Diode)
- Optimal wavelenght (630nm)
- Reduced illumination time (15mn)
- Touchscreen operating system
- Integrated RFID technology
- Full GMP-Procedure
- CE Marked by December 2007



MacoPharma

MacoTronic B2

Plasma illumination device for the THERAFLEX-MB Plasma pathogen reduction process

Ref. 9MB2000

Specifications :

Dimensions :	47 x 68 x 44 cm (width x depth x height).
Weight :	~ 35 kg
Power supply :	110-240V, 50-60Hz
Lighting system :	96 light-emitting diodes (LED), 4 modules of 24 LED each, 2 modules per bag (double-side exposure)
Wave length :	627 +/-10 nm
Connectivity :	4 USB ports (rear panel : 3, front panel : 1), 1 Ethernet port (network connection)
Screen :	5,5 inch VGA colour touch screen
Cooling system :	Ventilation of illumination chamber by laminar air flow

- **Operating mode :**

Delivered energy :	Preset as per THERAFLEX-MB Plasma procedure
Bag loading mode :	Manual opening of the drawer
Capacity per cycle :	2 bags per cycle
Temperature of use :	Air-conditioned room (20-22°C)

- **Operating controls :**

Light sensors :	4 control photo-diodes (1 per light module)
Temperature sensors :	2 pyrometers for direct measurement on each bag surface and for ambiant temperature in the illumination chamber
Alarms :	Flashing logo for operating status, sound alarm for errors

- **Process control & traceability :**

Barcode reading :	Bag ID and batch, product code, operator, post-labelling barcode control
Report printing :	Cycle illumination report providing energy, intensity and temperature records
Cycle record :	Up to 8000 illuminations files stored in the internal memory
Backup :	Transfer of illumination files by USB key or MacoTrace (Data Manager)
Network connection :	TCP/IP protocol, assignable IP adress through MacoTrace
Import/export :	Connection to the IT Management System (LIS) through MacoTrace

- **Accessories :** USB barcode laser reader, thermal transfer label printer, report printer, MacoTrace licence, ethernet cable, RFID module

- **Regulations :**

CE Marking :	Conformity with MDD 93/42/EEC expected for end Q1 2008
Electrical safety :	Conformity with EN 61010-1 expected for end Q1 2008
Electromagnetic certification :	Conformity with EN 61326-1 expected for end Q1 2008

9MB2000_A_C 22/02/2008

Certified ISO 9001 Certified ISO 13485
MacoPharma
F - 59420 MOUVAUX

First investigations on a newly developed LED illumination device for the treatment of MB-plasma

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Purpose

Treatment of fresh frozen plasma (FFP) with MB (methylene blue) and light is a procedure used for the inactivation of blood-borne viruses for more than 15 years. MB plasma is currently produced in several European countries using the MacoPharma Theraflex MB plasma system. High-intensity, long-lived light-emitting diodes (LEDs) are now available on the market, which might replace the sodium vapour lamps currently used in the Macotronic device (MacoPharma). The purpose of this study was the first evaluation of a newly developed LED illumination device (picture 1) with respect to virus inactivation capacity and plasma quality.

Picture1: Prototype

Methods

Picture 2: Pre-series device

Treatment was done in the Theraflex MB plasma bag system (MacoPharma), containing leucocyte-depletion filter Plasmaflex, MB pill (85 µg MB), illumination bag, MB depletion filter Blueflex and plasma storage bag. For investigating plasma quality 3 plasma pools were each prepared from 3 different single donor units. Plasma was divided into three illumination bags and illuminated on the LED device. Samples were taken at different time points of illumination and factor VIII and fibrinogen (Clauss) were determined.

For investigating virus inactivation capacity Pseudorabies virus (PRV) was spiked into FFP (n = 4) resulting in a titer of approximately 10^6 tissue culture infectious doses/ml ($TCID_{50}$/ml). The viral titer was determined from samples taken after 5, 10, 15 and 20 minutes of illumination on the LED device. Infectivity was determined by endpoint titration using a Vero cell CPE (cytopathic effect) assay. In a preliminary run the currently used Macotronic was compared with the newly developed LED device.

Results

Virus inactivation was investigated using the PRV, an enveloped, double-stranded DNA virus, which is used as model virus for HBV. MB/light treatment using the LED-based illumination device resulted in an inactivation of > 4 log steps of PRV after 10 – 15 min of illumination (diagram 1). The device is at least as effective as the Macotronic device routinely used at present.

Table 1: Inactivation kinetics of PRV (n = 4)

sampling time [min]	0	5	10	15	20
log_{10} $TCID_{50}$/ ml (mean ± SD)	6.16 ± 0.23	4.64 ± 0.68	≤ 2.41 ± 1.65	≤ 1.75 ± 0.38	≤ 1.54 ± 0.00
log_{10} reduction factor		1.52	≥ 3.75	≥ 4.41	≥ 4.62

Plasma quality was only slightly affected by illumination. Factor VIII was decreased by 17% and fibrinogen (Clauss) by 14% during an illumination of 20 min (Diagram 2). Results are at least comparable to or might even be better than those for the Macotronic device.

Diagram 1: Inactivation of PRV by LED device (n=4) and Macotronic (n=1)

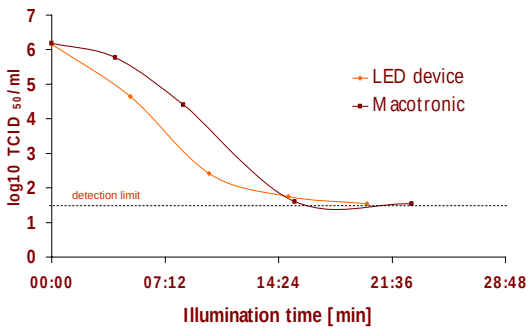
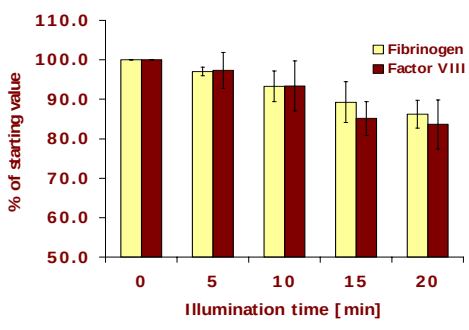


Diagram 2: Influence on coagulation factors (n = 3)



Conclusions

A new, compact illumination device based on long-lived LEDs was developed. The preliminary data suggest that this LED device is comparable to the Macotronic device with respect to virus inactivation capacity and preservation of plasma quality. Illumination time might even be shortened by using this high intensity illumination device.

Three years' haemovigilance of methylene blue-treated fresh frozen plasma : no increase in transfusion reaction incidence

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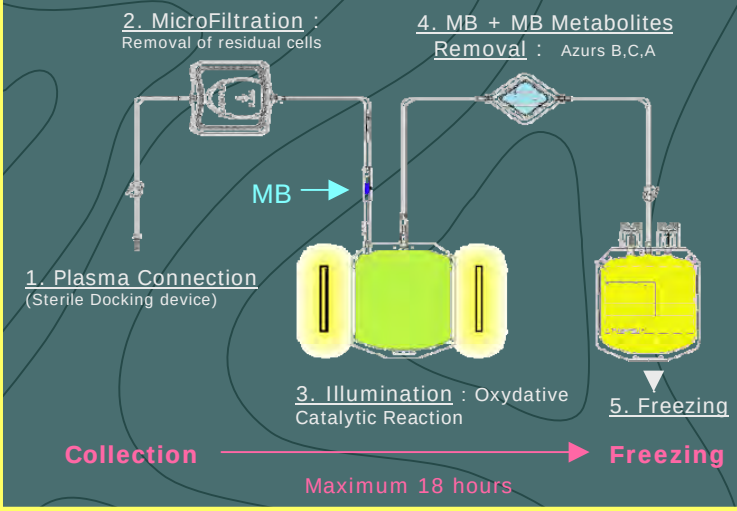
Background

Due to stringent donor selection, laboratory testing and pathogen inactivation procedures, fresh frozen plasma (FFP) offers a high degree of viral safety. In Belgium, only non remunerated volunteers are recruited as plasma, platelets and blood donors. Pathogen inactivation is a proactive strategy designed to inactivate a pathogen before it enters the blood supply. Methylene blue-photoinactivation was choosen by the Belgian Red Cross two years ago (Theraflex MB plasma – MacoPharma)

MB-viroinactivation (Theraflex-MB plasma MacoPharma)



Methods

Until mid 2004, only solvent-detergent FFP (SD-FFP) was used in our teaching hospital. BM-FFP began to be transfused to our patients thereafter. Since nearly 10 years, all transfusions of labile blood products are checked for the appearance or not of an adverse event.
In this study, the incidence and the seriousness of adverse event after BM-FFP transfusion were compared with those observed with SD-FFP.

Results

(a) : benign allergic reaction (n=4)
moderate allergic reaction (n=1)
NHFR (n=1)
(b) : benign allergic reaction (n=5)
moderate allergic reaction (n=3)
No TRALI episode (any previous pregnancy / transfusion = contra-indication for plasma donation)

	SD-FFP	BM-FFP
Period	2003 – 2004	mid 2004 – 2005
Number of FFP units transfused	5101	5660
Number of adverse reactions after FFP Tf°	6 (a)	8 (b)
Incidence of reaction	0.12 %	0.14 %

Discussion and conclusion

No significant increase in adverse event incidence was observed after BM-FFP transfusion (odds ratio 1.2) and the seriousness of these events was comparable. The clinical efficacy of both FFP was similar : both procedures have limited effects on coagulation factors (especially on fibrinogen and factor VIII for MB, on protein S and alpha 2-antiplasmin for SD).
Finally, plasma pooling may have the undesirable effect of increasing the risk of transmitting viruses that are either resistant to the process or have escaped the virucidal process.
The hallmarkof MB technology is that it allows the viral inactivation of single donor units of FFP, offering reassurance that no increased infectious risks are added due to pooling.
This a crucial point in term of public health safety.