



Initial single-center experience of Optia WBC Version 5 software in 24 consecutive autologous PBSC collection procedures, compared with a control group of 24 procedures using the COBE Spectra MNC setting



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Spectra Optia® - some background



Spectra Optia cell separator platform for plasma exchange



- The COBE Spectra® cell separator, initially developed in the 1980s, currently remains the world market leader for therapeutic apheresis
- CaridianBCT, who manufacture Spectra, have been keen to introduce recent technological improvements to improve on the Spectra platform
- A new cell separator machine, called “Spectra Optia®”, has recently been developed. This has a number of potential advantages over the older Spectra, including:
 - Smaller, lighter machine
 - Automated interface monitoring
 - Graphical, touch-screen user interface
- Although it shares many features of the older Spectra platform, it also shares features of the existing Trima system for donor platelet apheresis, which is a well-established and widely used system worldwide
- Spectra Optia obtained “CE Marking” (European regulatory approval) for HPC-A (PBSC) collection in January 2008, but FDA approval for US use is still pending



Our Unit - some background



SNBTS Clinical Apheresis Unit, Glasgow



- We are currently Scotland's largest therapeutic apheresis facility, performing approximately 1500 apheresis procedures per annum, of which about 30% are HPC-A (PBSC) collections
- We were involved both in initial pre-marketing evaluation of Spectra Optia® for PBSC collection, and in the European Compassionate Use Programme for plerixafor
- We became aware that cryopreservation volume was a frequent issue when collecting PBSC post-plerixafor using the MNC setting on COBE Spectra
- On introduction of Spectra Optia for PBSC collection, we noted that the effect of plerixafor on cryopreservation volume seemed much less marked



An initial positive experience with Optia WBC in Glasgow – ASH abstract Nov 2010



825 Significantly Lower Cryopreservation Volumes for PBSC Collections Using Spectra Optia® Version 5 Software Compared with the MNC Setting on COBE® Spectra, Particularly When Using Plerixafor for Mobilisation

Oral and Poster Abstracts

Oral Session: Cell Processing II

Monday, December 6, 2010: 6:45 PM

315 (Orange County Convention Center)

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Plerixafor (Mozobil®, Genzyme), an antagonist of the alpha chemokine receptor CXCR4, is highly effective as a novel PBSC mobilisation agent for patients failing to mobilise PBSC by conventional means, and is now licensed for this indication in Europe and the USA. However, significantly larger cryopreservation volumes have been reported as a disadvantage when plerixafor is used as part of PBSC mobilisation regimes (Tanhehco et al., Journal of Clinical Apheresis 2010, advance online publication). Although not an insurmountable problem in our own experience, this does increase liquid nitrogen freezer space requirements and also increases DMSO exposure for the patient at the time of re-infusion. In the course of a pre-marketing audit of the Version 5 PBSC collection software for the new Spectra Optia® apheresis platform (CaridianBCT), we observed significantly lower cryopreservation volumes for plerixafor collections when using Spectra Optia® than when using the widely-used mononuclear cell (MNC) setting (“Version 4.1”) on the conventional COBE® Spectra (Caridian BCT) apheresis platform. Formal audit was carried out of a series of 21 consecutive aphereses for PBSC procurement from 16 patients where plerixafor had been used as part of the conditioning regime, with Spectra Optia® being used for 10 procedures and COBE® Spectra for 11. Cryopreservation volume was strikingly and significantly lower for the Spectra Optia® procedures (median 351 mls; range 170 – 716 mls) than for COBE® Spectra procedures (median 756 mls; range 524 – 2400 mls; $p < 0.001$). Extension of this audit to a comparator group of 26 procedures on a temporally matched series of 18 consecutive patients where plerixafor was **not** used as part of the conditioning regime, of which Spectra Optia® was used for 7 procedures and COBE® Spectra for the remainder, did show lower cryopreservation volume for non-plerixafor collections compared with the 22 plerixafor collections though this did not reach statistical significance ($p = 0.11$). The total white cell count was noted to be significantly higher on the day of PBSC collection for the plerixafor group (median WCC $29.8 \times 10^9/l$) compared to the non-plerixafor group (median WCC $15.1 \times 10^9/l$; $p < 0.001$). Slightly lower cryopreservation volumes were seen in the non-plerixafor group when comparing the Spectra Optia® procedures to the COBE® Spectra procedures, but this was not statistically significant (median for Optia 354 mls, range 99-668 mls compared with median for Spectra 488 mls; range 298-954 mls; $p > 0.05$). However, comparison of Spectra Optia® collections with COBE® Spectra collections for all 47 procedures (plerixafor plus non-plerixafor collections) showed significantly lower cryopreservation volumes for Spectra Optia® ($p < 0.01$). Initial results with Spectra Optia® have shown that it yields a purer product than COBE® Spectra MNC, with lower granulocyte contamination, while maintaining the high PBSC collection efficiency of COBE® Spectra MNC (CaridianBCT, personal communication). In our experience, this translates into a greater than 50% reduction in median cryopreservation volume in the context of collection procedures where plerixafor is used as part of the conditioning regime, probably because of the higher total peripheral WCC seen in plerixafor-mobilised patients which leads to significant granulocyte contamination of the product with older cell separator platforms. Spectra Optia® therefore shows great promise as a solution to the problem of higher cryopreservation volumes when using plerixafor.

- Our initial clinical experience with Optia WBC for autologous PBSC collection has been positive
- We found that Optia gave significantly lower cryopreservation volumes than the MNC setting on Spectra, particularly for PBSC collections performed after plerixafor
- This was presented in abstract at ASH 2010
- We were keen to confirm these findings in a larger comparative audit of Optia WBC versus Spectra MNC, and also to compare other performance measures between the two systems



Design for current audit

- Audit was carried out on a series of 24 consecutive autologous PBSC collections on 18 patients performed on Optia MNC (either Version 5 pre-marketing software or initial production software post-marketing) over a period of 5 months
- As a comparator group, a series of 24 temporally matched autologous PBSC collection procedures were audited from a series of 15 patients who underwent PBSC collection on COBE Spectra (MNC setting) during the same five-month period
- Data collected for each procedure included:
 - Patient parameters: gender, age, total blood volume, diagnosis
 - Patient's total WCC on day of collection
 - Procedure collection efficiency (calculated using peripheral CD34+ count on day of collection, volume of blood processed and CD34+ cell dose collected)
 - Procedure run time
- Additionally, patient and operator acceptability for Optia was assessed by brief informal survey
- Engraftment was reviewed for transplanted patients



Patient Characteristics



	OPTIA GROUP	SPECTRA GROUP	
	n=18	n=15	
Age (median; range)	56 (27-67)	62 (30-69)	p=n.s.
Gender distribution	7F:11M	5F:10M	p=n.s.
Diagnoses	12 MM; 5 lymphoma; 1 GCT	8 MM; 7 lymphoma	p=n.s.
Total blood volume (median; range)	4903 mls (3055-6160 mls)	4402 mls (3310-6520 mls)	p=n.s.
Total WCC on day of collection (x 10⁹/litre)	21.35 (9.4 – 38.7)	11.6 (1.7 – 27.2)	p<0.01

- Patients appeared well matched by age, gender, diagnosis and TBV
- However, the total WCC on day of collection was significantly higher in the Spectra group
- Of which, more later!!



Results – Collection Efficiency



- Collection efficiency was calculated for each individual procedure (as per normal Unit policy)
- Calculated as “CE2”, i.e. based on pre-run CD34+ count only
- CE2 = (Cells collected) / (Cells processed)
- = (Absolute CD34+ cell dose in bag) / (Peripheral CD34+ count x Volume of blood processed*)
 - *Volume of blood processed with citrate anticoagulant subtracted
- For Spectra procedures, “Volume of blood processed” is Final Inlet Volume minus Final AC Volume, from “End Run Results” screen
- For Optia procedures, “Volume of blood processed” is available with anticoagulant volume already subtracted in End of Run Summary.



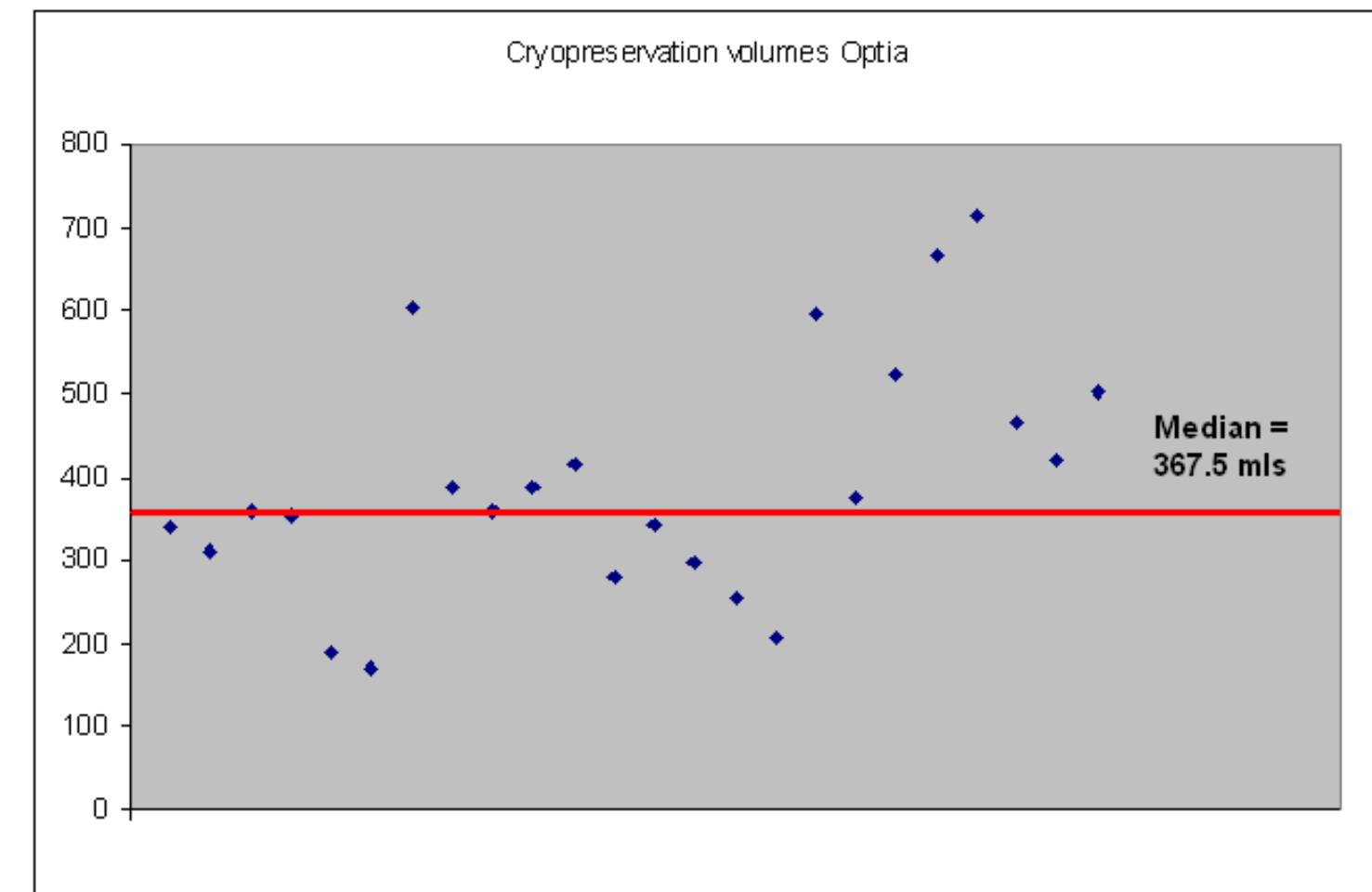
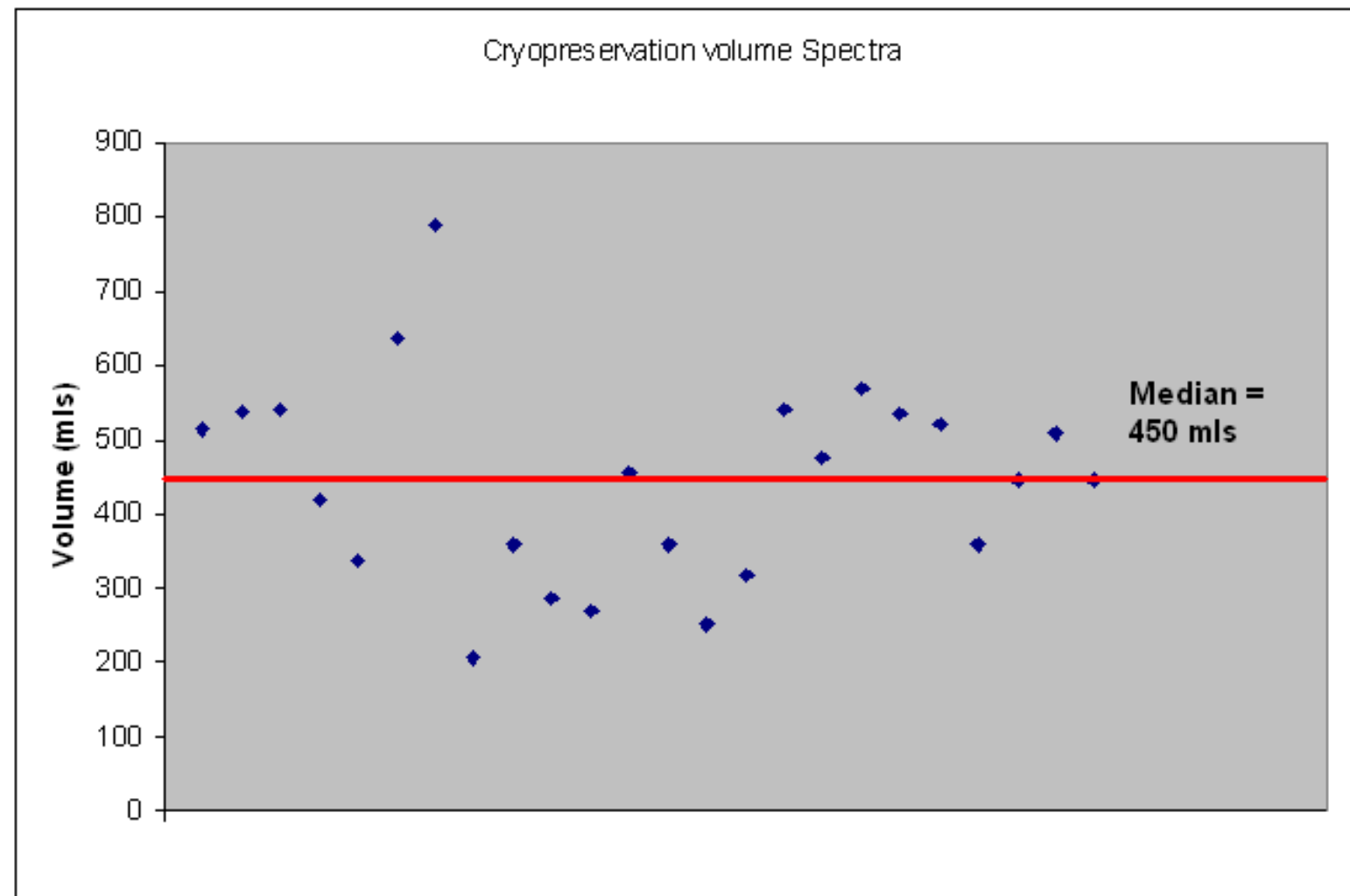
Results – Collection Efficiency (Continued)



- Median CE2 for 24 Optia procedures = **48.5%** (range 28.3 – 75.3%)
- Median CE2 for 24 Spectra procedures = **56.8%** (range 30% - 78.6%)
- Neither group is significantly different from our “benchmark” CE2 of **52%** for MNC procedures on COBE Spectra, determined from previous audit of more than 1000 Spectra procedures at our centre
- Nevertheless, the CE2 in the Spectra group is slightly higher than might be expected, and the CE2 in the Optia group slightly lower than might be expected, given previous published data suggesting that Optia has slightly higher Collection Efficiency overall compared with MNC procedure on Spectra¹
- There may be a relatively simple “non-machine” reason for this – of which, more later!!

1. Reinhardt P et al. Automatic interface-controlled apheresis collection of stem/progenitor cells: results from an autologous donor validation trial of a novel stem cell apheresis device. *Transfusion*, Epub ahead of print 2011, 2992 1..10

Results – Cryopreservation Volume



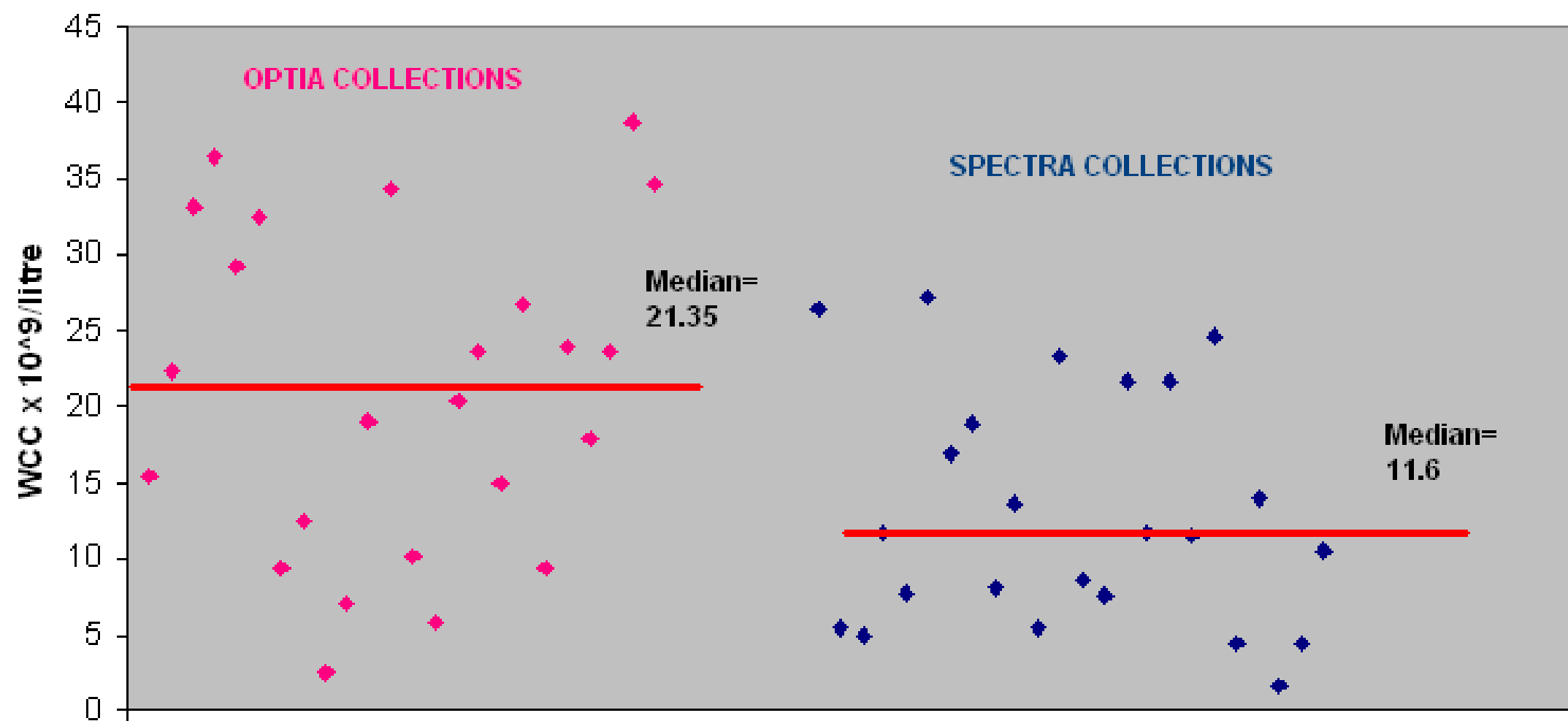
- Median cryopreservation volume was slightly lower for Optia procedures (367.5 mls) compared with Spectra procedures (450 mls), but this did not reach statistical significance
- This is in contrast to the strikingly lower cryopreservation volumes we had seen initially with Optia, as previously presented at ASH 2010
- Again, there may be a simple “non-machine” reason for this!



The Optia group had significantly higher WCC on the day of collection ... Why?



Total WCC for Optia collections compared to Spectra collections



- As a group, the Optia patients had a strikingly (and statistically significantly) higher WCC on the day of collection
- Why is this?
- We hadn't noticed it initially but it became obvious during data analysis



The Optia group had significantly higher WCC on the day of collection ... Why?



NON-MACHINE
FACTORS!



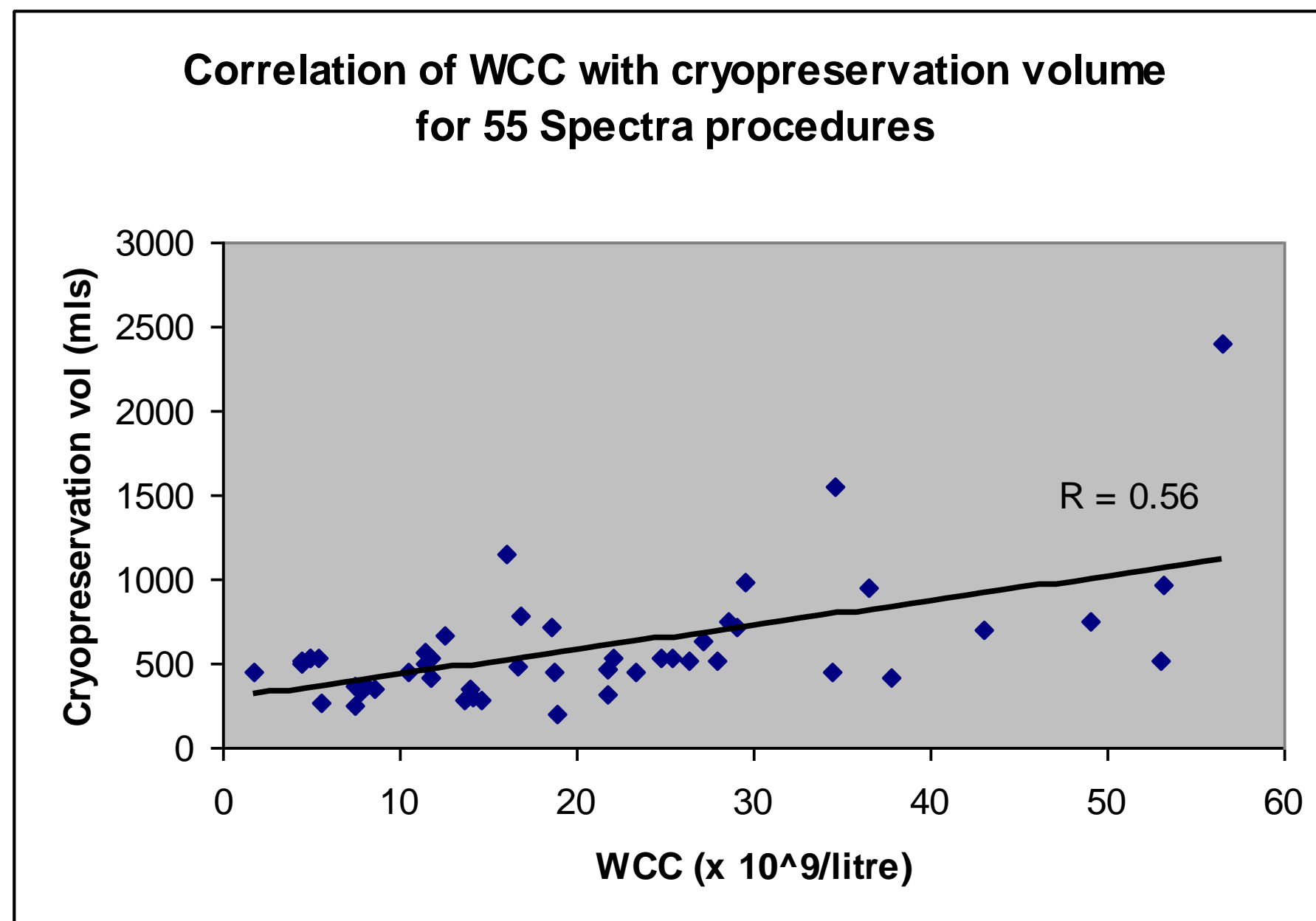
- We were already aware from our initial results that Optia appeared to have a useful effect of limiting cryopreservation volume when collecting on a higher WCC
- This had led us to adopt an “unofficial” unit policy of preferentially choosing Optia over Spectra when the patient’s day-of-collection WCC was on the high side
- This illustrates a genuine hazard of retrospective audits compared with RCTs
- We had inadvertently been giving Spectra all the “easier” procedures, and Optia all the “harder” procedures...!



The Optia group had significantly higher WCC on the day of collection ...



Why does this matter?



- We know from previous audit of Spectra procedures that there is a positive correlation between WCC on collection day and cryopreservation volume
- We also know that for Spectra, CE2 collection efficiencies tend to be lower on a higher WCC, and higher on a lower WCC
- By “giving” Optia patients with higher average WCCs, we would have expected to see higher cryopreservation volumes and lower CE2 in the Optia group, if the two machines were performing identically
- In fact, we saw slightly lower cryopreservation volumes in the Optia group

Higher cryopreservation volumes – why do they matter?

- Cells cryopreserved in multiple bags (can be as many as 21 bags) – this impacts on liquid nitrogen storage space
- Increased DMSO exposure, and potential DMSO toxicity, for patient at time of re-infusion
- Cells may have to be given back over several days – potential impact on engraftment times
- Increased lab staff time for processing of product
- Increased nursing time required for re-infusion of cells





Why are cryopreservation volumes lower with Spectra Optia® than with COBE Spectra?



Spectra Optia cell separator platform for plasma exchange



- The WBC (PBSC collection) system on Optia incorporates several novel features to try to increase product purity while maintaining the good CD34+ cell collection efficiency seen with the MNC setting on COBE Spectra

- These include:

- Automated Interface Management system

- Automated platelet recovery system (also has the effect of flushing granulocytes & granulocyte precursors out of the collected mononuclear cells)

- Overall effect is to reduce the Total Nucleated cell Count (TNC) in the product due to less contamination by granulocytes & granulocyte precursors

Other findings



- Optia procedures were slightly longer than Spectra MNC procedures on average (median procedure time 280 minutes on Optia vs. 250 minutes on Spectra, including rinseback time)

- Patient acceptability was good for both systems. During validation of 5 new Optia machines for PBSC collection, 20 out of 20 patients reported a positive experience of the machine overall.

- We have similar historical patient acceptability data for Spectra MNC.

- Operator acceptability was good for both systems

- Some operator comments:

“Optia is easier to move about than Spectra – the big wheels are a good feature”

“Optia can be a bit of a “princess” at first, but it is fine when you get used to it”

“The touch-screen is easy to follow – good for new operators”

“We don’t get embarrassed taking the machine into ITU any more for plasma exchanges!”





Engraftment figures for patients collected on Optia vs. Spectra



- Of the 33 patients, 3 did not proceed to autologous transplant (one in Optia group, 2 in Spectra group).
- Reasons were: significant co-morbidities (n=2); allograft instead due to positive post-treatment PET scan (n=1)
- Of the 30 patients receiving autologous transplant, 10 were transplanted with cells entirely collected on Optia, 12 with cells entirely collected on Spectra, and 8 patients received a mixture of Optia & Spectra cells

	Median days to n>0.5	Median days to n>1.0	
Optia cells only (n=10)	10 (10-12)	11 (10-12)	} No significant differences
Spectra cells only (n=12)	11 (9 - 23)	11 (10-N.E.)	
Mixture (n=8)	11.5 (10-13)	12.5 (10-13)	



Key Findings

- Despite the inadvertent confounding factor of higher day-of-collection WCC in the Optia group, our results are in keeping with our previous findings that Optia limits cryopreservation volumes when collecting on a higher WCC
- The “Optia effect” appears to be due to lower granulocyte contamination of the PBSC product, leading to lower TNC in the product and hence lower cryopreservation volume
- Collection Efficiencies are broadly comparable between Optia and Spectra MNC
- Engraftment times are not significantly different between cells collected on Spectra or Optia
- Optia is a viable replacement for Spectra as a PBSC collection platform