Hemopoietic Progenitor Cell Collection in Tandem with Hemodialysis for Patients with M-Protein Disorders

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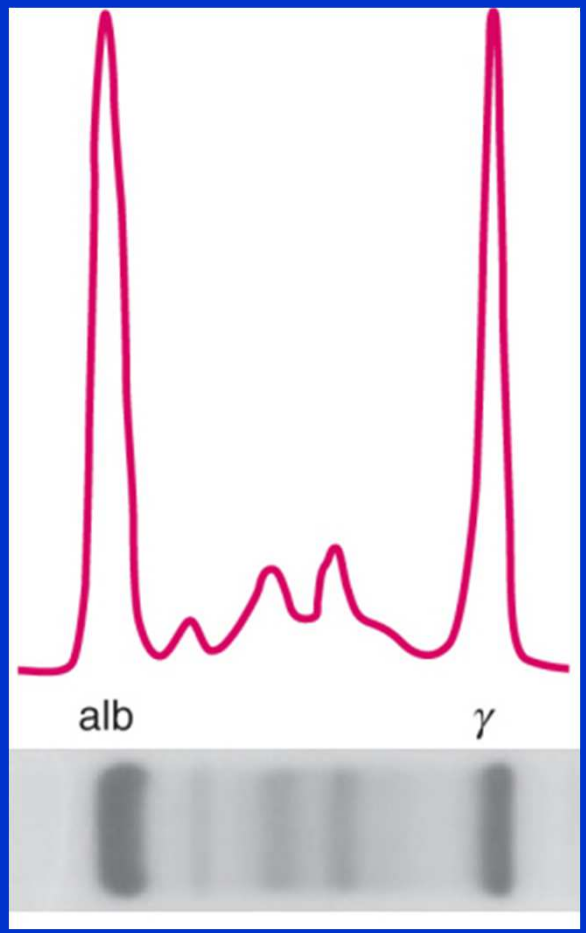
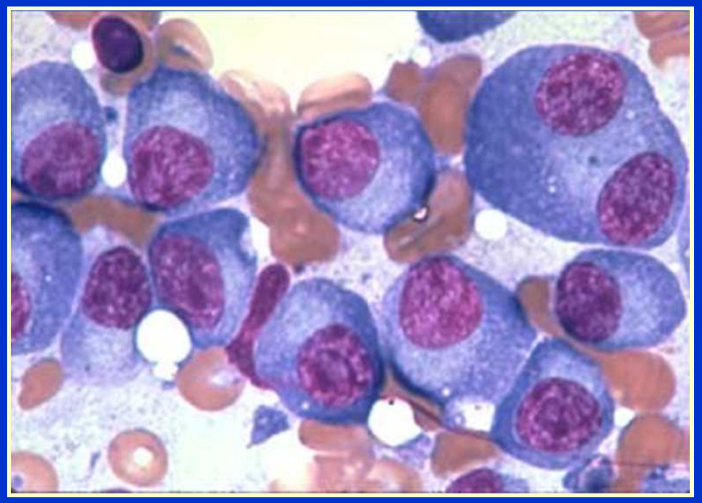
M-proteins and M-protein Disorders

- M-protein
  - Monoclonal immunoglobulin and/or free light chains
  - Produced by malignant clone of plasma cells
- M-protein disorders
  - Serum (plasma) M-protein
    - Renal impairment
    - Disordered Hemostasis
    - Altered plasma viscosity
  - Syndrome-specific clinical effects
    - Multiple myeloma
    - Amyloidosis
    - Waldenström's macroglobulinemia



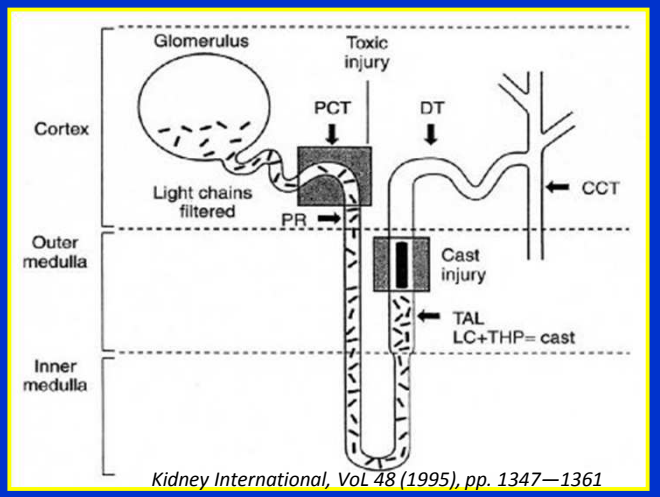
Multiple Myeloma

- Epidemiology
  - Median age 61♀, 62♂
  - 1-4 per 100,000 per year
  - 30,330 new US cases in 2016
  - 12,650 US deaths in 2016
- Renal Impairment
  - 20-40% at diagnosis
  - 10% need dialysis at diagnosis
- Median survival
  - Conventional treatment: 3-4 years
  - Auto HPC transplant: 5-7 years
- **Apheresis in multiple myeloma**
  - *Many will receive plasma exchange while also receiving hemodialysis*
  - *All will be offered autologous HPC collection, including those receiving hemodialysis*

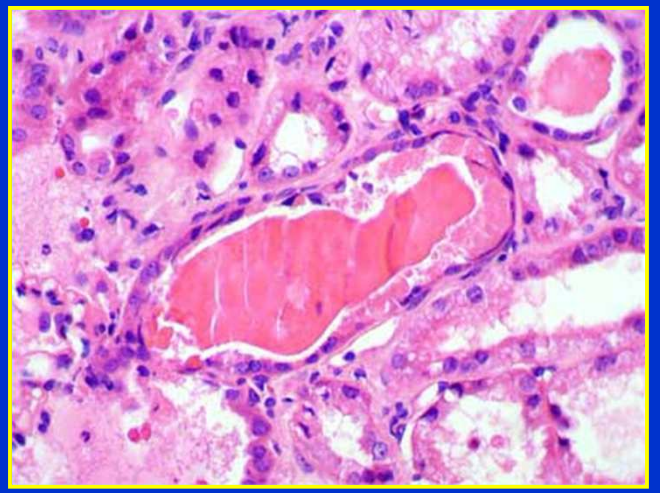


Renal Impairment in Multiple Myeloma

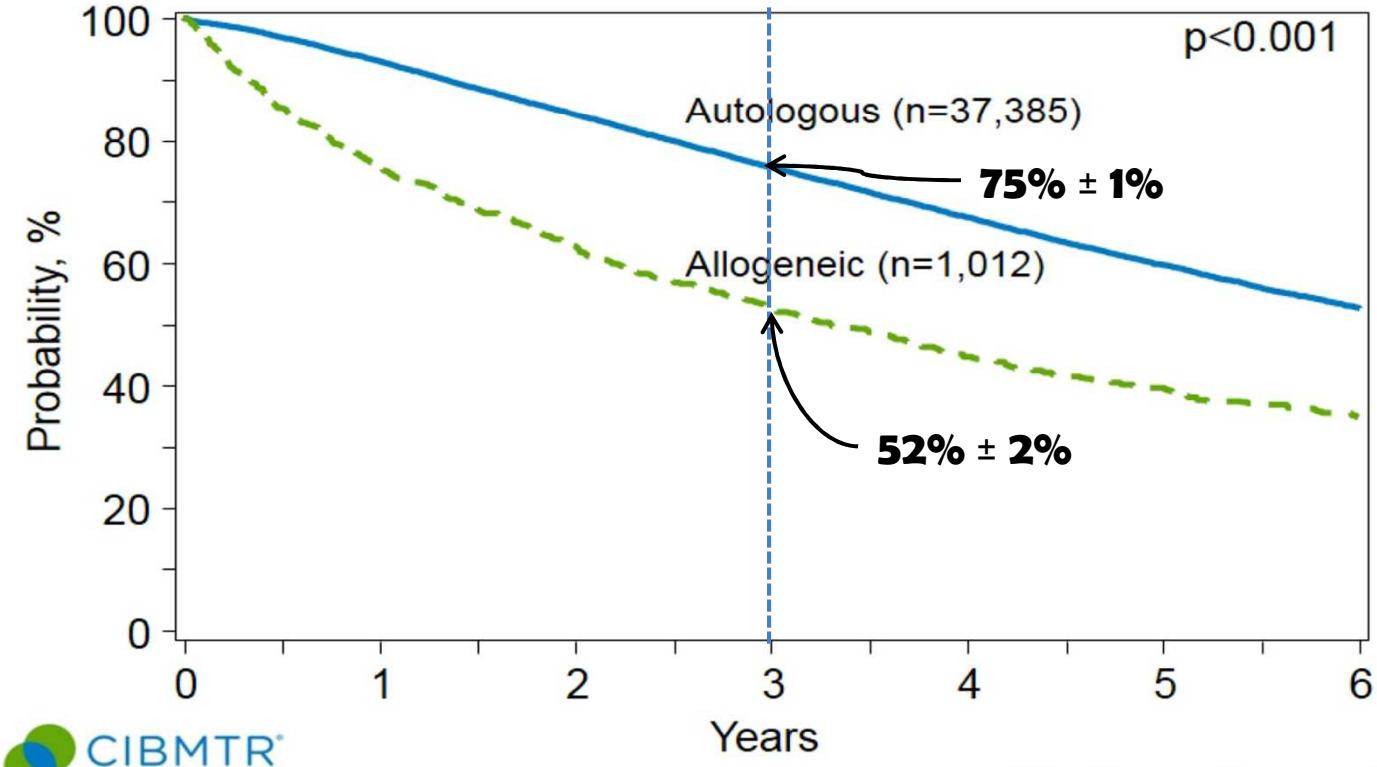
- Nephrotoxic effects of monoclonal light chains (LC)
  - *Cast nephropathy* ("myeloma kidney") in 90% of cases
    - PCT light chain receptors (megalin and cubilin) overwhelmed
    - Light chains combine with Tamm-Horsfall protein in distal tubules
  - Amyloidosis
  - Light chain deposition: PCT
    - Local stimulation of IL-6, TNFα by LC
    - Interstitial fibrosis
- Contributing factors
  - Dehydration
  - Hypercalcemia
  - Hyperuricemia
  - Drugs (NSAIDs, antibiotics)



Kidney International, Vol 48 (1995), pp. 1347—1361



Survival after Transplants for Multiple Myeloma, 2003-2013



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By Donor Type

Can Peripheral Blood HPC Collection be Performed in Tandem with Hemodialysis?

What would be the effect on

- Efficacy of the hemodialysis procedure
- Collection efficiency of hemopoietic progenitor cells
- Engraftment

Case Report (LA)

- 72 y/o ♂ with κ light chain myeloma
- Myeloma kidney requiring hemodialysis
- Poor response to initial chemotherapy
- Offered high intensity treatment
  - Intensive chemotherapy x 2
  - Autologous transplantation
    - Mobilization from course #2
    - HPC collection by apheresis

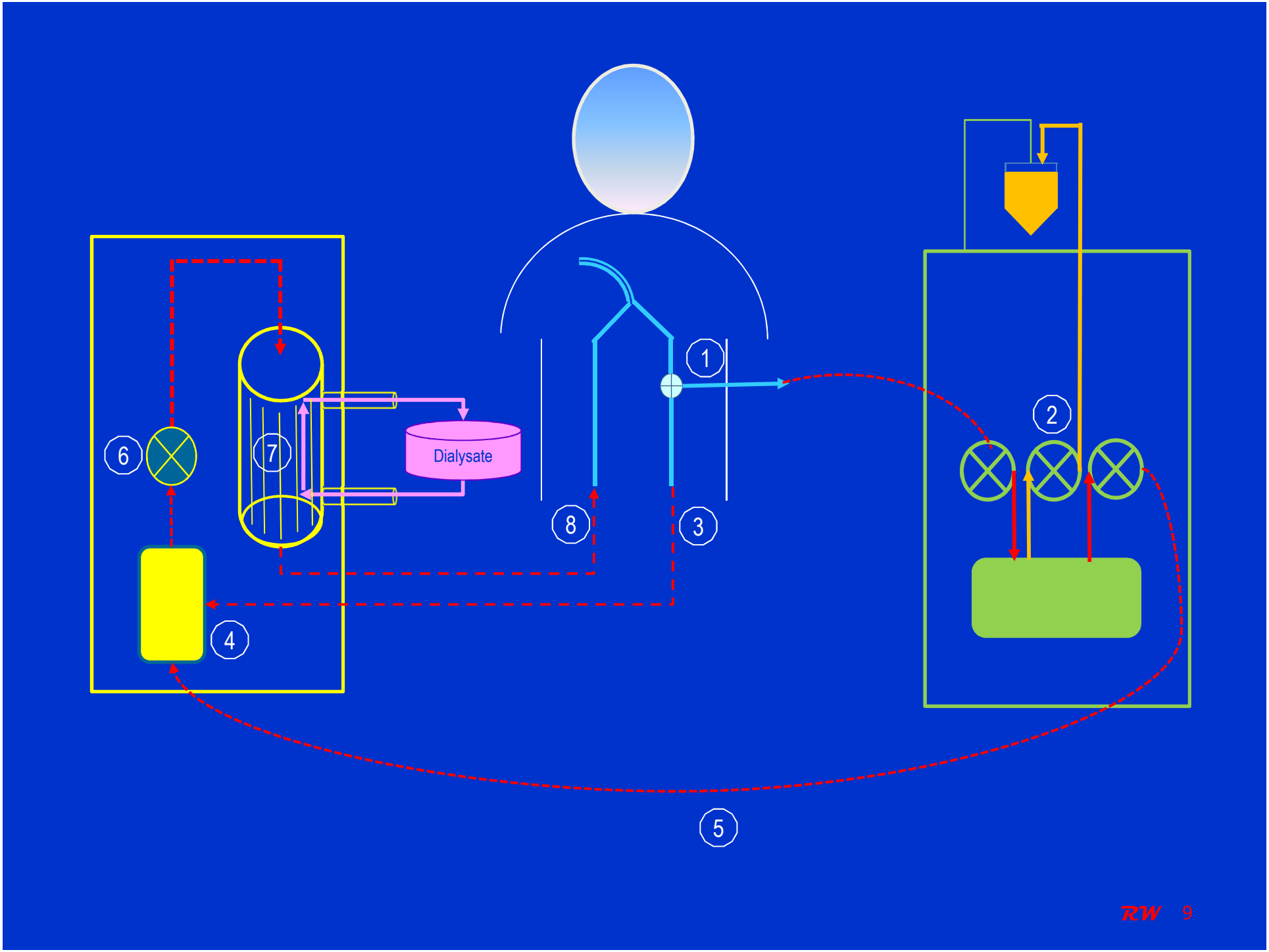
Apheresis and Hemodialysis Parameters

Apheresis Considerations

- Spectra LRS Turbo ver 7.0
- WBFR 80-100 ml/min
- Blood volumes processed limited by the duration of HD
- Anticoagulant
  - ACD-A 500 mL bags
  - 0.8 mL/min/L patient blood volume
  - Heparin 3000 U/bag ACD-A
- No supplemental calcium

Hemodialysis Considerations

- Gambro Phoenix 2
- Fresenius polysulfone dialyzer
- Electrolytes (mEq/L)
  - Na^+ 141
  - Ca^{++} 2.5
  - HCO_3^- 35
  - K^+ 2.0
- QB 300-400 ml/min
- 4 hour dialysis
- Laboratory parameters
  - BUN pre- and post-dialysis
  - $[Ca]_i$ pre- mid- and post-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Dialysate

Tandem HPC Collection and Hemodialysis

Outcome of Tandem HPC Collection and HD

Efficacy of hemodialysis (urea reduction ratio):

$$URR = 100 \times \frac{[BUN]_{PRE} - [BUN]_{POST}}{[BUN]_{PRE}}$$

Collection efficiency (CE) of hemopoietic progenitor cells:

$$CE = 100 \times \frac{[CD34^{+}]_{PROD} \times VOL_{PROD}}{[CD34^{+}]_{BLOOD} \times VOL_{BLOODPROC}}$$

- Hemodynamic stability of patient during tandem procedures
- Ionized calcium during the procedures
- Number of $CD34^{+}$ cells collected
- Engraftment

Clinical Characteristics of Patients

Patient	Age/Gender	M-Protein Disorder	Indication for Hemodialysis
LA	72 y/o ♂	κ light chain multiple myeloma	Cast nephropathy
JC	59 y/o ♂	κ light chain multiple myeloma	Cast nephropathy
FR	74 y/o ♂	λ light chain multiple myeloma with plasma cell leukemia	Cast nephropathy
SM	60 y/o ♀	IgG κ multiple myeloma with amyloidosis	Hypertensive renal disease and cast nephropathy

HPC Collection Parameters and Outcomes

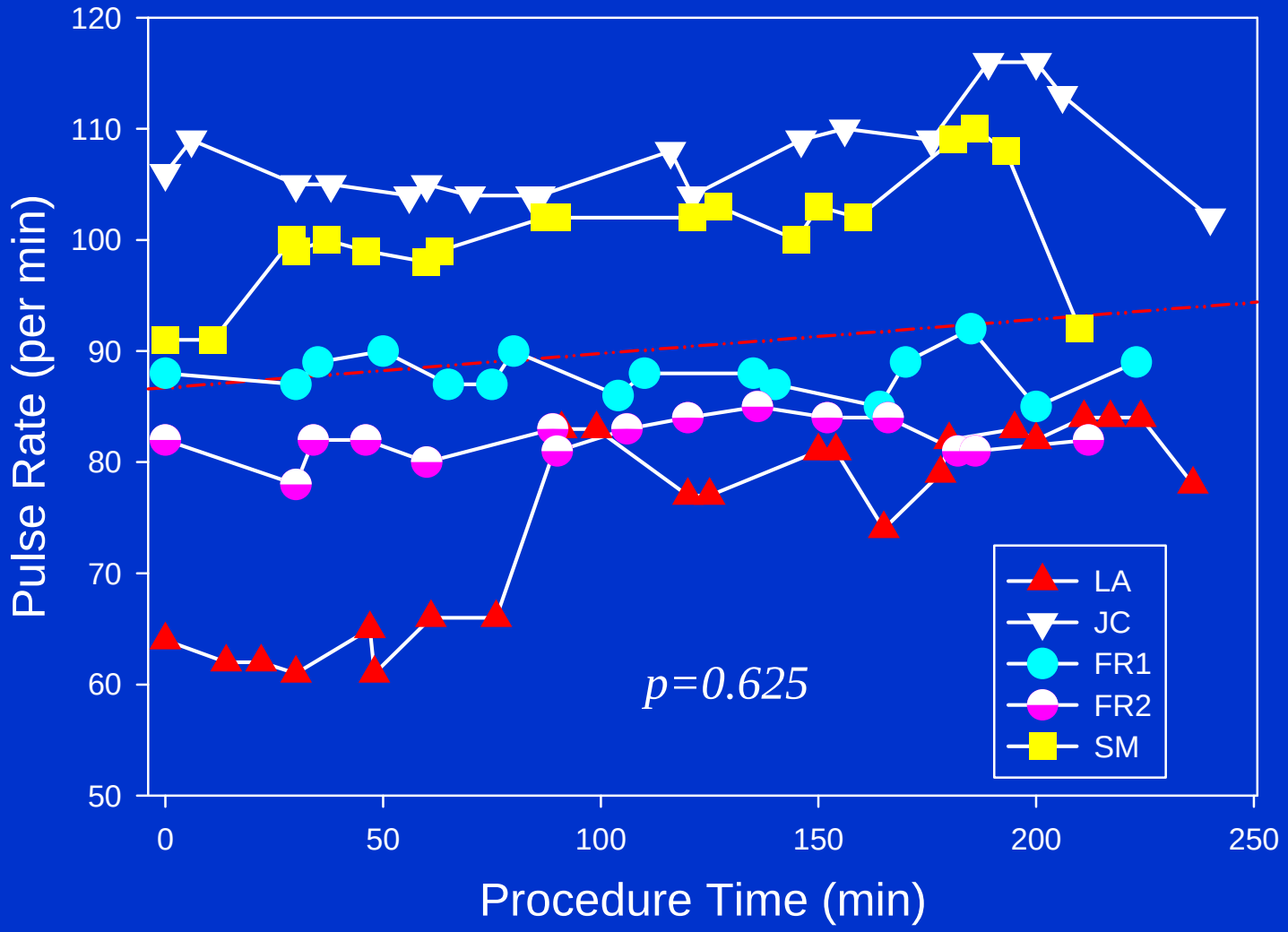
Pt	Blood Vol (L)	$CD34^+$ Count (per µL)	Collection Time (min)	Blood Volumes Processed	Product Volume (mL)	$CD34^+$ Collected ($x10^6$/kg)	$CD34^+$ CE (%)	URR (%)	Day of Engraft-ment
LA	4.655	48	212	3.84	407	8.93	70.7	73.9	11
JR	4.473	80	216	4.33	417	11.7	53	§	10
FR	6.675	16	181	2.7	347	1.91	84	62.5	‡
	6.643	57	185	2.77	355	5.45	65	67.7	
SM	3.350	88	244	4.63	366	6.38	27¶	73.4	‡

§ Not measured. BUN was 16 mg/dL on day of procedure.

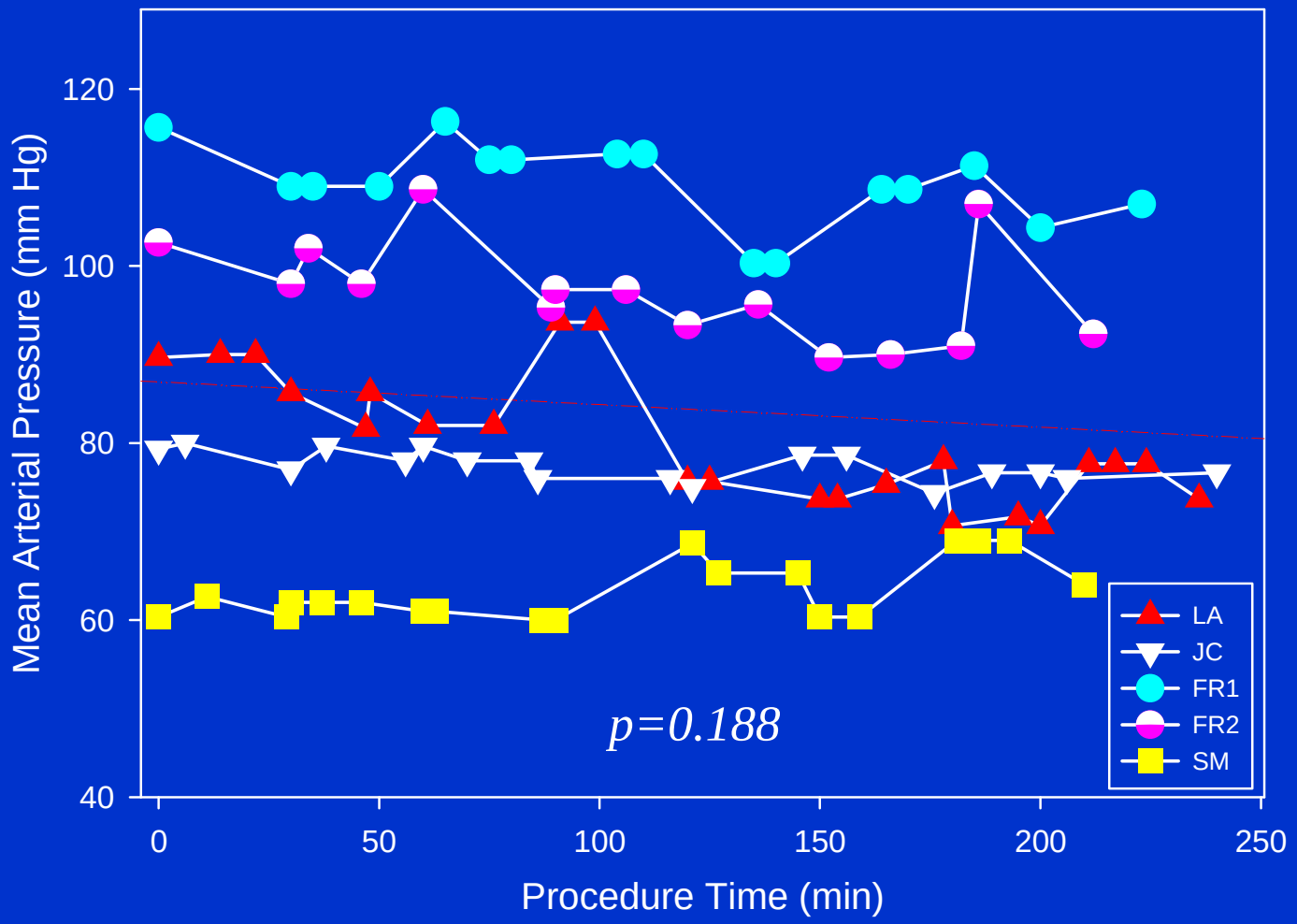
‡ Expired while awaiting hospitalization for autologous transplantation.

¶ Peripheral WBC count was 148.6 x 10^3/µL on the morning of collection procedure.

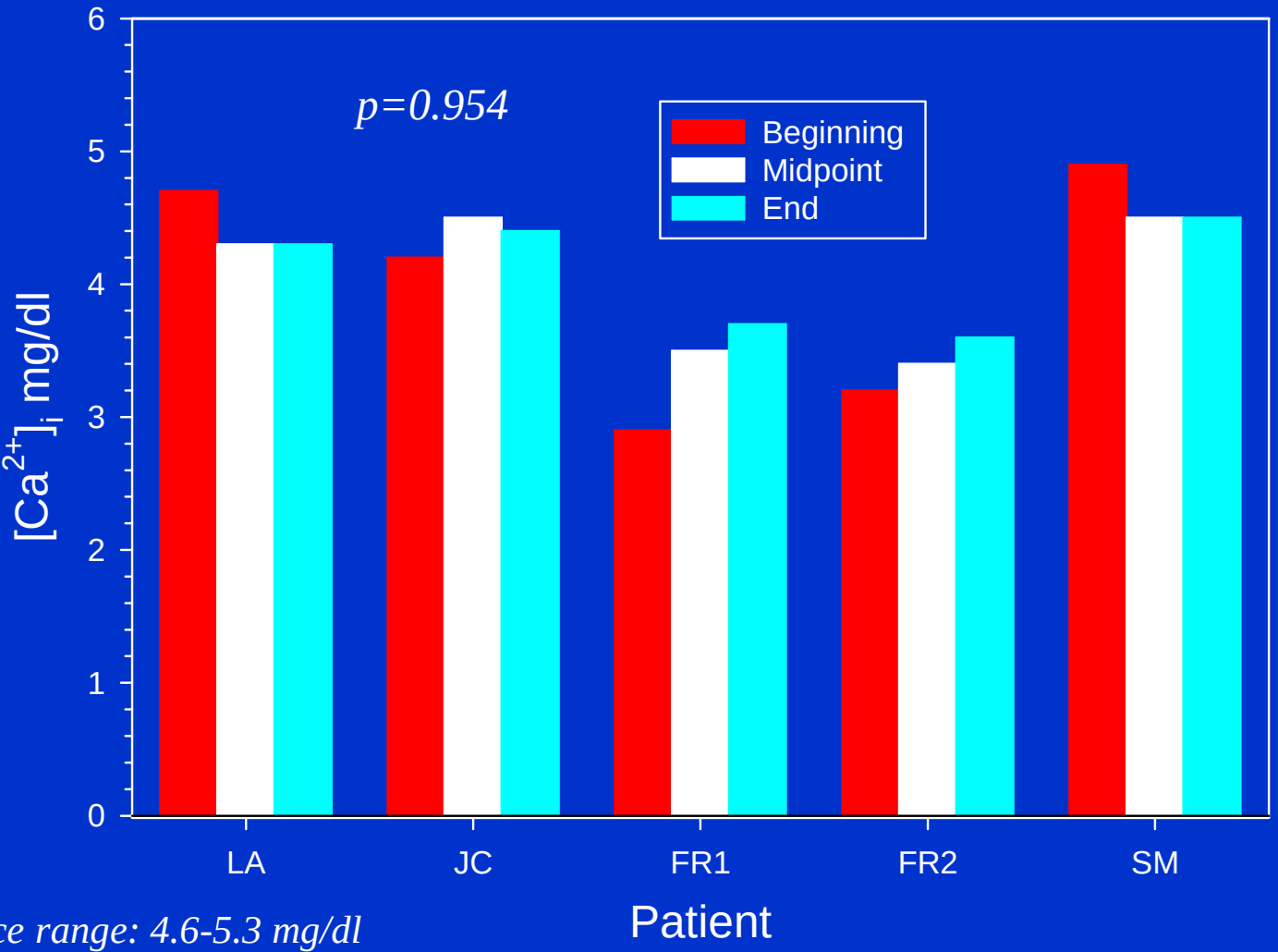
Pulse Rate Not Significantly Changed During Tandem HD/HPC Collection



Mean Arterial Pressure Remains Stable During Tandem HD/HPC Collection



Ionized Calcium Remains Stable During Tandem HD/HPC Collection



Reference range: 4.6-5.3 mg/dl

Tandem HD/HPC Collection

- HPC collection can safely be performed in tandem with hemodialysis
- Tandem procedures do not compromise the efficiency of HPC collection or the efficacy of hemodialysis
- Tandem-collected HPC engraft as expected
- Ionized calcium homeostasis is maintained by the hemodialysis