Multiple Myeloma: Quantitative Staging and Assessment of Response with a Programmable Pocket Calculator

By Sydney E. Salmon and Stephen B. Wampler

Studies of M-component synthesis and metabolism, as well as clinical staging of multiple myeloma, have provided the basis for calculation of the total body tumor cell number and quantitation of response to treatment. Many of the calculations involved have been complex and have previously required the availability of a computer. The advent of programmable pocket calculators has permitted simplification of these programs for general clinical and investigative applications in studies of myeloma and related monoclonal gammopathies. In this paper we have included the background information and a clinical example of the use of the programmable calculator, as well as the logic steps and the calculator programs themselves, for several of the most useful programs for clinical staging and quantitation of response to therapy in IgG myeloma.

QUANTITATIVE immunologic "marker" techniques (based upon M-component synthesis and catabolism) have been developed over the past decade by our clinical research group to measure tumor cell number[1,2] and the growth and regression of multiple myeloma.[3] In the course of this work we have also applied predictive techniques to analyze tumor kinetics[3] and to clinically stage patients with respect to tumor cell mass.[4] The predictive techniques all use readily obtainable clinical data and, in the cases with serum M components, have been shown to have very high correlation with measured M-component mass turnover[3] and total body tumor cell number.

In order to make this approach available to clinicians, the various computing routines and storage for patient files were initially integrated into a computer-based myeloma study system which could be accessed via a small terminal through a time-sharing computer network available in many countries.[5] The development of programmable pocket calculators (e.g., the HP-65, Hewlett-Packard, Cupertino, Calif., or the SR-52, Texas Instruments, Dallas, Texas) has permitted yet another step towards immediate solutions of relatively complex calculations. The purpose of this paper is to describe a simplified quantitative approach to staging and assessment of cell kill with chemotherapy for patients with IgG or IgA multiple myeloma (approximately 80% of all myeloma

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cases[6]) that uses a programmable hand calculator. We are currently carrying out immunologic studies on patients with pure Bence Jones myeloma (no serum M component); these have only recently been initiated and results cannot yet be assuredly predicted.

The programmable calculator is particularly desirable for analysis of response in cases with IgG myeloma (50% of all myeloma cases[6]) because of the complexities of IgG metabolism. Since these techniques are generalized and apply to the majority of patients, we recognize and caution that a few individual patients may deviate from these norms if they have major aberrances in M-component structure or metabolism. The user should be cautioned that metabolic data on the rare cases of IgG_3 myeloma (5%–8% of IgG cases) may not be calculated quite as accurately as the remainder of IgG and IgA cases. While the calculating routines which we use are probably also suitable for clinical calculations of the percent change in tumor cell number in IgG_3 cases, for those interested in protein research it is important to point out that the calculations underestimate the molecular turnover of IgG_3 protein.

Application of staging and assessment of response will be discussed in subsequent sections. Program routines for several of the HP-65 programs are provided in the appendix to this paper, as are simplified instructions for the program routines. Analogous programs for the SR-52 are available upon request from the authors.

MATERIALS AND METHODS

Equations for Clinical Staging in Multiple Myeloma

A simple system for predicting total body tumor cell mass in myeloma cases was recently developed by Durie and Salmon.[4] The regression equations shown in Table 1 were derived from stepwise multivariate regression analysis which correlated presenting clinical features singly and in combination with measured myeloma cell mass, with the optimal models chosen according to the value of the multiple correlation coefficient (R^2). The regression equations for predicting myeloma cell mass shown in Table 1 have been incorporated into the calculator programs. Since these equations require only simple arithmetic, a four-function calculator would also be sufficient. Relatively few IgA and Bence Jones cases have yet been analyzed; as more data become available more specific equations will be formulated for these specific categories.

When the programs for staging are utilized, the operator sequentially enters the scaled value for bone survey results and the numerical values for the laboratory parameters (e.g., hemoglobin, M component, calcium), as well as the patient's height (cm) and weight (kg). Results

Table 1. Regression Equations for Calculating Myeloma Cell Mass

A. IgG Myeloma (preferred equation for IgG cases)

Myeloma cell mass (cells $\times 10^{12}$)/m^2 = 0.413 + 0.256 × bone lesions*
+ 0.019 × urine M component − 0.059 × hemoglobin
+ 0.065 × serum calcium + 0.050 × serum M component

B. All Cases (useful for IgA, Bence Jones, and IgG cases)

Myeloma cell mass (cells $\times 10^{12}$)/m^2 = 0.601 + 0.283 × bone lesions*
+ 0.031 × urine M component − 0.058 × hemoglobin
+ 0.051 × serum calcium + 0.028 × serum M component

Adapted from Ref. 4.

*Bone lesions on skeletal X-ray survey are stated on a scale of 0 to 3: 0, normal bones; 1, osteoporosis only; 2, lytic bone lesions; 3, extensive skeletal destruction and major fractures. Values for laboratory tests are entered directly as hemoglobin (g/100 ml), serum M component (g/100 ml), serum calcium (mg/100 ml), and urine M component (g/24 hr).

are available as both the patient's myeloma cell mass $\times 10^{12}/m^2$ and total myeloma cell number ($\times 10^{12}$) (the calculator computes the patient's body surface area from height and weight).

Equations for Calculation of Percentage Change of Tumor Size in Serum M-Component Cases

For IgG, IgA, IgD, or IgE myeloma cases, the fractional tumor regression can be calculated from the serum M-component concentration, height, weight, and (when available) plasma volume. The same technique is applicable in macroglobulinemia for IgM, but then plasma volume data are essential. For IgA cases (and probably IgD and IgE), the fractional catabolic rate appears to be fixed,[7] and the fractional change in serum M-component concentration is a reasonable estimate of the change in tumor mass, unless there has been a significant change in plasma volume. In our experience, plasma volume does fall significantly in myeloma patients who respond to treatment after presenting initially with high serum M-component concentration and/or hyperviscosity. Similarly, patients who present with severe anemia may also have increased plasma volumes that return towards normal as the hemoglobin rises in association with response to treatment. It is therefore our practice to obtain ^{131}I-albumin plasma volumes on serum M-component cases initially and at 6-mo intervals in order to assess this variable. Programs for calculating response are designed to use plasma volume when this information is available or to assume a fixed 3.5-liter plasma volume when it is not.

For IgG cases, a complex calculation is necessary because the fractional catabolic rate varies as a function of serum concentration. The equation of Waldmann and Strober[7] has been incorporated, as was also the case in our prior kinetic analyses:[3]

$$f = a - \frac{D}{Vc + mD}$$

where f is the fractional catabolic rate, a is the fraction of the plasma pool isolated per day, D is the number of molecules protected from catabolism per unit time at full saturation, Vc is the total circulating IgG pool (the product of the serum IgG concentration c and the plasma volume V), and m is the slope of a plot of the milligrams of IgG predicted ($[Vc(a-f)]^{-1}$) against the reciprocal of the plasma pool of IgG, $(Vc)^{-1}$. From our clinical studies[3] we have estimated 0.16 as the value of a and, as did Waldmann and Strober,[7] have used 147 mg/kg/day as the value for D. With calculated initial and followup values for f for IgG, then the percentage change in myeloma tumor mass, ΔM, can be calculated as

$$\Delta M = 100 \times [(C_f \times V_f \times f_f)/(C_i \times V_i \times f_i) - 1],$$

where C is the serum M-component concentration and where the subscripts f and i indicate follow-up and initial values, respectively. As with the IgA cases, if V has not been measured, it is assumed to be constant.

When a serum IgG M-component spike is small (e.g., less than 2.0 g/100 ml), it is important to distinguish between the monoclonal IgG and normal IgG for purposes of correct calculation of f (on the basis of total IgG), with the value for f then applied to calculation of the specific IgG M-component turnover rate. This step is required because the rate of catabolism of subpopulations of IgG molecules is governed by the total serum IgG concentration.[7] A more accurate value for the monoclonal fraction can be calculated from the total IgG and the proportion of IgG in the spike areas. When the total serum IgG is relatively low, total IgG can be determined from the total area in the gamma region on serum electrophoresis or from the value for total IgG by immunodiffusion. We tend to rely more heavily on electrophoretic values, since they can be analyzed geometrically and since the concentrations of IgA and IgM are sufficiently low to have negligible influence on the total gamma area. [We believe that electrophoretic values are also generally more reliable in the high range for myeloma patients. In our experience, radial immunodiffusion sometimes gives inconsistent results at high M-component concentrations and is therefore better for measuring nonmyeloma immunoglobulins.] A specialized program for low gamma concentrations that is suitable for the pocket calculator has been written for this purpose. The low-gamma program includes entry of initial and followup values for total IgG and the geometry of the M-component area in the gamma region. The program logic for this special circumstance is included in Fig. 1. We consider it best for investigators to become familiar with

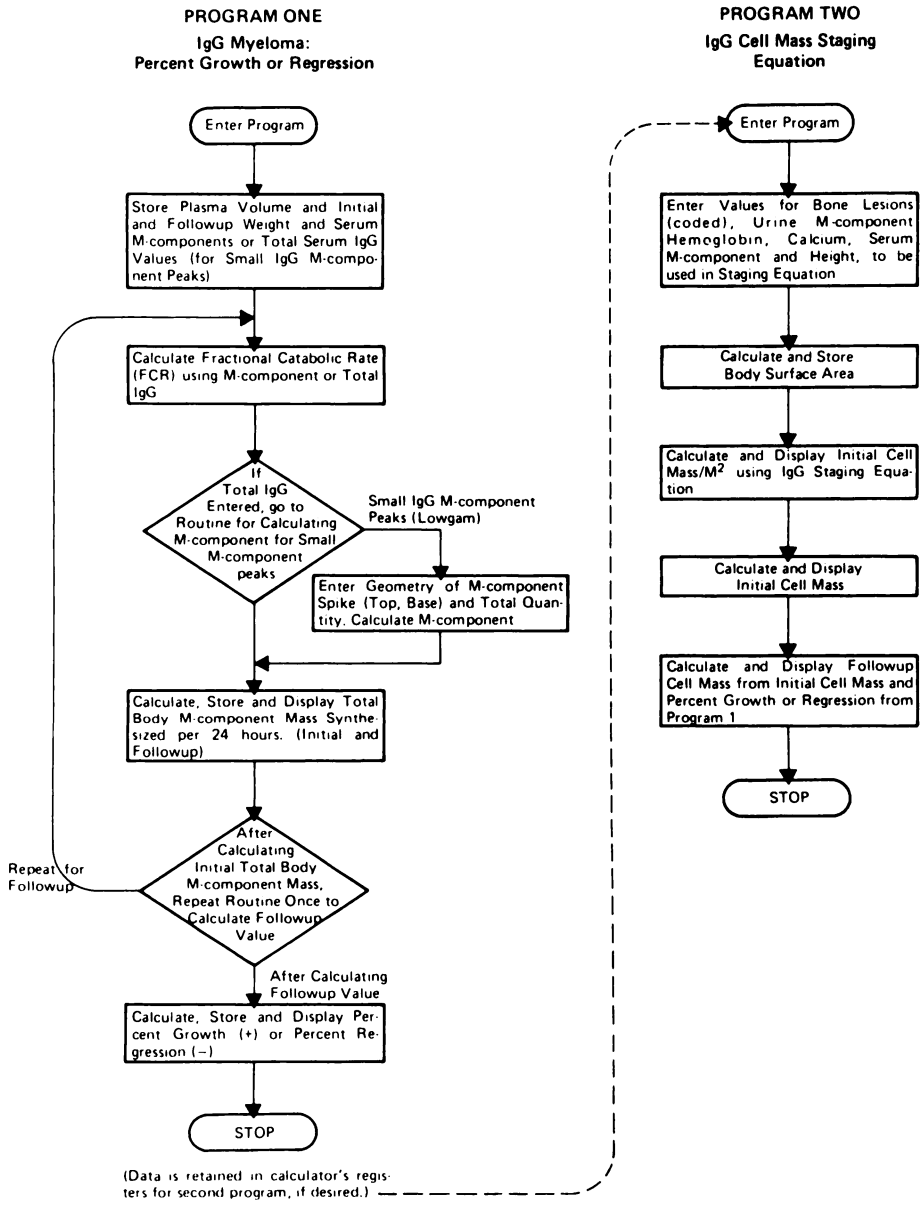

Fig. 1. Flow diagram of program logic for the sequential programs for (1) calculation of percentage growth or regression and (2) total tumor mass staging in IgG myeloma. The additional steps for the specialized low-gam program required for patients with small M-component peaks are also included within (1).

the use of the general program first (see Appendix, program I) and to then use the low-gamma program when they find need for it (see Appendix, program III).

For serum M-component cases other than IgG (IgA, IgM, IgD, IgE), direct keyboard calculation is sufficient, because the fraction catabolic rate is fixed; this is basically a calculation of the percentage change in the circulating pool of the M component,

$$\Delta M = 100 \times [(C_f \times V_f)/(C_i \times V_i) - 1],$$

where ΔM is the percentage change in tumor mass. For research purposes (and convenience) we have included the fractional catabolic rates for IgA, IgM, IgD, and IgE in one program analogous to that for calculating growth/regression in IgG cases. This program (available from the authors) calculates the total body M-component synthetic rate for these clones and is useful in conjunction with the staging program or with direct measurements of the immunosynthetic rate per myeloma cell in vitro for calculation of the total body tumor cell number.[1,2]

Calculation of Change in Total Body Tumor Mass

Given the calculation of percentage change in tumor size, plus the prediction of quantitative tumor burden from the regression equation, it becomes a simple matter to calculate the change in absolute tumor mass (this approach can, of course, be used both for tumor regression and tumor growth):

follow-up tumor mass = initial tumor mass × fractional change in tumor size,

where the initial tumor mass is calculated from the regression equation and the fractional change in tumor size = (% change)/100 + 1.

For IgG cases, all of the above calculations have been incorporated into two sequential program cards which can be used to calculate (1) fractional change in tumor size (growth or regression) and (2) initial tumor mass ($\times 10^{12}$) (see Appendix, program II). A flow diagram showing the logical steps in these programs is shown in Fig. 1.

EXAMPLE: CASE REPORT

A 63-yr-old patient presents with bone pain and weakness and has diagnostic findings of myeloma, including an IgG M component and 45% plasma cells in the bone marrow. The bone X-rays show several lytic lesions (scale 2), the hemoglobin is 9.6 g/100 ml, the serum M component concentration is 4.4 g/100 ml, and the serum calcium is 11.5 mg/100 ml. A 24-hr urine electrophoresis shows no evidence of an M component (0 g/24 hr). The patient weighs 64 kg and his height is 165 cm.

The patient is then treated with melphalan-prednisone and has relief of bone pain, a rise in the hemoglobin concentration, and improved appetite. Four months later the patient weighs 66 kg and the serum M-component has fallen to 1.8 g/100 ml (a 59% fall in M-component concentration). The plasma volume is not measured.

Description of program

(1) *Enter fractional tumor mass program:*
Initialize
Enter initial weight, initial M-component concentration
Enter follow-up weight, follow-up M-component concentration
First answer: initial total IgG mass synthesized = 17.91 g (24 hr)
Second answer: percentage growth or regression = −70.78% (regression)
Third answer: follow-up circulating IgG mass = 5.23 g (24 hr)

(2) *Enter staging program*
Initialize
Enter bone lesions, urine M component, hemoglobin, serum calcium, serum M component, patient's height
First answer: Myeloma cell mass × 10^{12} cells/m^2 = 1.33
Second answer: Absolute myeloma cell mass × 10^{12} cells = 2.29 × 10^{12} cells

(3) *Calculate effect of treatment on total body tumor burden*
Initial tumor mass (from staging program) = 2.29 × 10^{12} cells
Follow-up tumor mass = 6.69 × 10^{11} cells (70.8% regression)

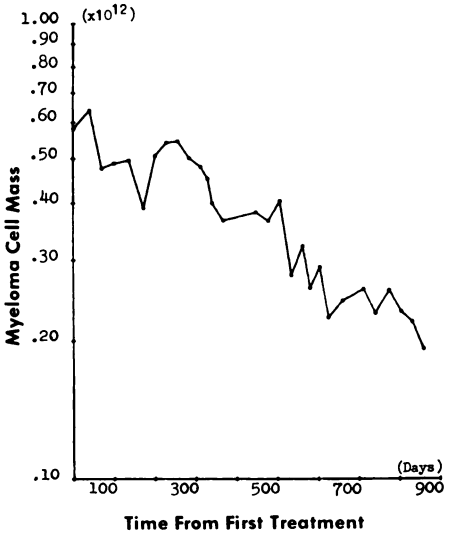

Fig. 2. Serial tumor mass values calculated from clinical data for a 67-yr-old man with IgG multiple myeloma. The patient was treated at 4-wk intervals with several alkylating agent combinations during the initial 250 days with only a transitory tumor regression and relapse with recurrent symptoms. At that point, treatment was changed to the combination of Adriamycin (Adria Laboratories, Wilmington, Del.) and BCNU with prompt relief of symptoms and progressive fall in total body tumor mass, which has continued up to the time of latest follow-up on June 21, 1976.

DISCUSSION

This approach to the quantitative assessment of clinical response literally requires less than 5 min for an individual case, given a handy programmable pocket calculator and the patient's medical record. We have used the pocket calculator for this purpose on numerous occasions while seeing individual patients in follow-up clinic, as well as when analyzing data on flow sheets in protocol studies. This approach is particularly useful for assessment of response with pilot studies in our own institution. Given this type of quantitative data for 10–15 patients, one can be reasonably certain of the efficacy of a new treatment. We have used this general approach (with the myeloma study system) in analyzing our quite favorable experience with the combination of BCNU/Adriamycin in patients in relapse[8] and have found an excellent correlation between presenting tumor mass, the magnitude of tumor response, and survival.[4] A series of serial calculations can be used for preparing a plot of an individual patient's clinical course, as shown in Fig. 2. We therefore recommend its use to clinicians and investigators with particular interest in plasma cell neoplasia and hope that this approach will receive widespread independent testing.

Note: After this paper had been prepared manufacture of the HP-65 was discontinued and the model replaced with a newer version (the HP-67). Only minor changes in programs are necessary for conversion to the newer calculator, since it uses the same logic as the HP-65. The authors will make programs modified for the HP-67 available to the readers.

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APPENDIX

We give HP-65 calculator user instructions and program forms for (1) IgG myeloma mass calculation and percentage growth/regression, (2) prediction of total tumor mass (initial and follow-up) in patients with IgG myeloma, and (3) a program particularly useful for following

IgG myeloma patients who have only small residual M-component peaks (< 2.0 g/100 ml) after treatment and have some recovery of normal immunoglobulins. The last program is applicable to M-component peaks as small as 0.3 g/100 ml. The second program can be altered to stage all cases by substituting the constants shown in Section B of Table 1 for those that were included from Section A. For IgG cases the equation from section A of Table 1 is more accurate. Throughout these programs PPL is the M-component concentration (g/100 ml) and PV is the plasma volume (liters).

PROGRAM I. MYELOMA CELL MASS CALCULATION AND PERCENTAGE GROWTH/REGRESSION IN IgG MULTIPLE MYELOMA

HP-65 User Instructions

Step	Instructions	Input Data (Units)	Keys	Output Data
I	Clear all stacks		f STK	
II	Load in program card			
III	A. Key in wt 1, press "A"	Wt 1 (Kg)	A	Wt 1
	Key in PPL 1, press "R/S"	PPL 1 (g/100 ml)	R/S	PPL 1
	Key in wt 2, press "R/S"	Wt 2 (Kg)	R/S	Wt 2
	Key in PPL 2, press "R/S"	PPL 2 (g/100 ml)	R/S	3.5
	B. Optional: PV has been set to 3.5 liters at this point. If you wish to use a different value, key in PV, press "D"	PV (liters)	D	PV
IV	A. Press "B" to calculate mass 1		B	Mass 1
	B. Optional: To alter PV at this point for second mass value, key in PV, press STO 7; otherwise, go to step IV C	PV (liters)	STO 7	PV
	C. Press "R/S" to calculate mass See displayed percentage growth/ regression = 100 * (M2/M1 − 1). Note: growth is +, regression is −		R/S	Growth/Regression
V	Press "C" to view mass 1		C	Mass 1
	Press "R/S" to view mass 2		R/S	Mass 2

Note: After completion, you may load the myeloma staging program by clearing program memory *only* and loading staging program.

HP-65 Program Form

Key Entry	Code Shown	Comments
fLBLA	31	Key "A" for data entry
	23	
	11	
STO 1	3301	Enter wt 1
R/S	84	
STO 2	3302	Enter PPL 1
R/S	84	
STO 3	3303	Enter wt 2
R/S	84	
STO 4	3304	Enter PPL 2
3.5	03	
	83	PV = 3.5
	05	
STO 7	3307	
RTN	24	
fLBLB	31	Key "B" calculates mass 1, stops, waits
	23	for new PV, then calculates mass 2
	12	and percentage growth/regression
RCL 1	3401	
STO 8	3308	
RCL 2	3402	
STO 9	33	
	09	
E	15	Calculate mass 1
STO 5	3305	
R/S	84	Wait for new PV to be loaded into R7

HP-65 Program Form (*cont.*)

Key Entry	Code Shown	Comments
RCL 3	3403	
STO 8	3308	
RCL 4	3404	
STO 9	33	
	09	
E	15	Calculate mass 2
STO 6	3306	
RCL 5	3405	
÷	81	
1	01	
−	51	X = 100 * (M2/M1 − 1)
100	01	
	00	
	00	
*	71	
STO 9	33	
	09	
RCL 1	3401	
STO 8	3308	
RCL	34	
9	09	
RTN	24	
fLBLC	31	Key "C" displays first mass 1,
	23	then mass 2
	13	
RCL 5	3405	

HP-65 Program Form (*cont.*)

Key Entry	Code Shown	Comments
R/S	84	
RCL 6	3406	
RTN	24	
fLBLE	31	Subroutine "E" returns
	23	X = mass, given wt in R8,
	15	PPL in R9, PV in R7
RCL 8	3408	
147	01	
	04	
	07	
*	71	
EEX 4	43	
	04	
RCL 7	3407	
*	71	
RCL 9	34	
	09	
*	71	
955.5	09	
	05	
	05	
	83	
	05	
RCL 8	3408	
*	71	

HP-65 Program Form (*cont.*)

Key Entry	Code Shown	Comments
+	61	
÷	81	
.16	83	
	01	
	06	
g x ≶ y	3507	
−	51	
EEX 1	43	
	01	
RCL 7	3407	
*	71	
*	71	
RCL 9	34	
	09	
*	71	
RTN	24	
fLBLD	31	Key "D" stores a new PV value into R7
	23	
	14	
STO 7	3307	R7 ← PV
RTN	24	

Registers: R1, wt 1; R2, PPL 1; R3, wt 2; R4, PPL 2; R5, mass 1; R6, mass 2; R7, PV; R8, used by program to pass; R9, "E" for wt & PPL.

PROGRAM II. MYELOMA STAGING (IgG CASES EQUATION)

HP-65 User Instructions

Step	Instructions	Input Data (Units)	Keys	Output Data
I	Load Program			
II	Enter data			
	A. Coded bone lesions	BL (coded)	A	
	B. Urine M component	UPL (g/24 hr)	R/S	
	C. Hemoglobin	Hgb (g/100 ml)	R/S	
	D. Serum calcium	Ca (mg/100 ml)	R/S	
	E. Serum M component	PPL (g/100 ml)	R/S	
	F. Height	Ht (cm)	R/S	
III	If program I or III was run immediately prior to this, skip to IV			
	A. Enter wt	Wt (kg)	STO 8	
	B. Enter growth/regression (%) (for regression input %, key CHS for −)	Gro/Reg (%)	STO 9	
IV	Press "B", read initial cell mass/m^2		B	$CM1/m^2$
	A. Press R/S, read actual cell mass		R/S	CM1
	B. Press R/S, read second cell mass		R/S	CM2

CM, cell mass.

Note: The patient's body surface area (BSA) may be displayed after step IV by recalling register 1 (key RCL 1).

Note: By changing the contents of specific registers and executing step IV, program will repeat using changed values. See register list for contents of various registers. You may not change R1 (BSA) directly, since BSA is recalculated by IV each time "B" is pressed.

HP-65 Program Form

Key Entry	Code Shown	Comments
f	31	Data entry function
LBL	23	
A	11	
STO 2	3302	Bone lesions (BL)
R/S	84	
STO 3	3303	Urine M component (UPL)
R/S	84	
STO 4	3304	Hgb (Hb)
R/S	84	
STO 5	3305	Calcium (Ca)
R/S	84	
STO 6	3306	Serum M component (PPL)
R/S	84	
STO 7	3307	Ht
RTN	24	
f	31	Result calculation function
LBL	23	
B	12	
.	83	$BSA = 0.0235 * Ht^{0.42246} * Wt^{0.51456}$
0	00	
2	02	
3	03	
5	05	
RCL 7	3407	
.	83	
4	04	
2	02	
2	02	
4	04	
6	06	
g	35	
y^x	05	
*	71	
RCL 8	3408	
.	83	
5	05	
1	01	
4	04	
5	05	
6	06	
g	35	
y^x	05	
*	71	
STO 1	3301	
.	83	Staging equation:
4	04	$CM/m^2 = 0.413 + 0.256(BL) +$
1	01	$0.019(UPL) - 0.059(Hb) +$
3	03	$0.065(Ca) + 0.050(PPL)$
Enter	41	
.	83	

HP-65 Program Form (cont.)

Key Entry	Code Shown	Comments
2	02	
5	05	
6	06	
RCL 2	3402	
*	71	
+	61	
.	83	
0	00	
1	01	
9	09	
RCL 3	3403	
*	71	
+	61	
.	83	
0	00	
5	05	
9	09	
RCL 4	3404	
*	71	
−	51	
.	83	
0	00	
6	06	
5	05	
RCL 5	3405	
*	71	
+	61	
.	83	
0	00	
5	05	
0	00	
RCL 6	3406	
*	71	
+	61	End of staging equation
R/S	84	Display $CM1/m^2$
RCL 1	3401	
*	71	
R/S	84	Display CM1
RCL	34	
9	09	
1	01	
0	00	CM2 = CM1 * (% growth/100 + 1)
0	00	
+	81	
1	01	
+	61	
*	71	
RTN	24	Display CM2

Registers: R1, BSA; R2, BL; R3, UPL; R4, Hgb; R5, Ca; R6, PPL; R7, Ht; R8, Wt; R9, growth/regression (%).

PROGRAM III. MYELOMA CELL MASS CALCULATION AND PERCENTAGE GROWTH/REGRESSION IN IgG MYELOMA (INCLUDING "LOW GAM")

HP-65 User Instructions

Step	Instructions	Input Data (Units)	Keys		Output Data
I	Clear all stacks		f	STK	
II	Load in program card				
III	Store initial values for:				
	(a) Wt 1	(Kg)	STO	1	
	(b) PPL1 or total gamma 1*		STO	2	
	(c) Wt 2	(Kg)	STO	3	
	(d) PPL2 or total gamma 2†		STO	4	
	(e) PV	(liters)	STO	7	
IV	Press key "A" to start		A		
V	When 1.00 appears on display:				
	• If value is not low gam, clear flag 1		f^{-1}	SF1	
	and proceed to VI by advancing program		R/S		
	• If value is low gam, set flag 1		f	SF1	
	and continue by advancing program		R/S		
	(a) when 2 appears, enter spike top*	Spike top	R/S		
	(b) when 3 appears, enter spike base	Base	R/S		
	(c) when 4 appears, enter spike	Spike	R/S		
VI	Program will display CM1 and stop.				
	To enter a new PV:	PV (liters)	STO	7	
	To continue with mass 2:		R/S		
	Repeat step V.				
	After V (second time) the growth/regression (%) is displayed (growth is +, regression −)				
	To view CM1:		RCL	5	Cell Mass 1
	To view CM2:		RCL	6	Cell Mass 2
	To view growth/regression (%):		RCL	9	Gro/Reg (%)

Similar to program I, but with an additional routine for calculation of samples with small M-component peaks ("low gam") wherein the metabolic rate for the M component is governed by the total IgG concentration, much of which is non-M-component.

*Registers 2 and 4 hold the serum M-component values if the program is not to use the low-gam equations. If the program is to use low gam, then registers 2 and 4 hold the total gamma globulin value. The total gamma value can be obtained by integrating the total area in the gamma globulin region on electrophoresis, or from the value for IgG from radial immunodiffusion assay (the latter is not useful for high levels). The "spike top" and "spike base" are determined graphically from the electrophoretic pattern and can be expressed in millimeters or number of boxes in the given area on the graph paper. Spike top is the area in the "spike" which sits on top of the "base" of normal gamma globulin immediately below it on the electrophoresis. "Spike base" thus refers only to the immediate area beneath the spike top, and not the entire gamma globulin zone.

†After completion, program II for myeloma staging can be loaded in as it is after program I.

HP-65 Program Form

Key Entry	Code Shown	Comments
LBL	23	Key "A" calculates cell masses and
A	11	growth/regression (%)
RCL 1	3401	Load wt 1 from R1
STO 8	3308	
RCL 2	3402	Load PPL (gam) 1 from R2
STO	33	
9	09	
E	15	Calculate mass 1
STO 5	3305	
R/S	84	Accept new PV
RCL 3	3403	Load wt 2 from R3
STO 8	3308	
RCL 4	3404	Load PPL (Gam) 2 from R4
STO	33	
9	09	
E	15	Calculate mass 2

HP-65 Program Form (*cont.*)

Key Entry	Code Shown	Comments
STO 6	3306	
RCL 5	3405	Calculate growth/regression (%)
÷	81	
1	01	
−	51	
1	01	
0	00	
0	00	
*	71	
STO	33	Store data for chaining to staging
9	09	program
RCL 1	3401	
STO 8	3308	
RCL	34	Display growth/regression (%)
9	09	
RTN	24	

HP-65 Program Form (*cont.*)

Key Entry	Code Shown	Comments
f	31	Internal subroutine to calculate
LBL	23	cell mass
E	15	
RCL 8	3408	Equation (a): $f = 0.16 - [(147 * wt)/$
1	01	$(PPL * PV * 10^4 + 955.5 * wt)]$
4	04	
7	07	
*	71	
EEX	43	
4	04	
RCL 7	3407	
*	71	
RCL	34	
9	09	
*	71	
9	09	
5	05	
5	05	
.	83	
5	05	
RCL 8	3408	
*	71	
+	61	
÷	81	
.	83	
1	01	
6	06	
g x ≶ y	3507	
−	51	
EEX	43	Equation (b): $X = f * PV * 10$
1	01	
RCL 7	3407	
*	71	
*	71	
STO 8	3308	
1	01	Stop for control; if flag 1 set, obtain
R/S	84	low-gam information

HP-65 Program Form (*cont.*)

Key Entry	Code Shown	Comments
f	31	
TF1	61	
1	01	
GTO	22	
2	02	
LBL	23	
1	01	
RCL 8	3408	Equation (d): CM = PPL * X
RCL	34	
9	09	
*	71	
RTN	24	
LBL	23	
2	02	
2	02	Equation (c): low-gam PPL =
R/S	84	spike * top/(top + 2 * base)
Enter	41	
Enter	41	
3	03	
R/S	84	
2	02	
*	71	
+	61	
÷	81	
4	04	
R/S	84	
*	71	
STO	33	Replace gamma with PPL
9	09	
GTO	22	
1	01	

Registers: R1, wt 1; R2, PPL1 or gamma 1; R3, wt 2; R4, PPL 2 or gamma 2; R5, Mass 1 × 10^{12}; R6, Mass 2 × 10^{12}; R7, PV; R8, internal; R9, growth/regression (%).

REFERENCES

1. Salmon SE, Smith BA: Immunoglobulin synthesis and total body tumor cell number in IgG multiple myeloma. J Clin Invest 49:1114-1121, 1970

2. Salmon SE: Immunoglobulin synthesis and tumor kinetics of multiple myeloma. Sem in Hematol 10:135, 1973

3. Sullivan PW, Salmon SE: Kinetics of tumor growth and regression in IgG multiple myeloma. J Clin Invest 51:1697-1708, 1972

4. Durie BGM, Salmon SE: A clinical staging system for multiple myeloma. Cancer 36:842, 1975

5. Salmon SE, Durie BGM: Cellular kinetics in multiple myeloma—A new approach to staging and treatment. Arch Intern Med 135:131-138, 1975

6. Hobbs JR: Immunochemical classes of myelomatosis. Br J Haematol 16:559, 1969

7. Waldmann TA, Strober W: Metabolism of immunoglobulins. Prog Allergy 13:1-110, 1969

8. Alberts DS, Durie BGM, Salmon SE: Doxorubicin/BCNU chemotherapy for multiple myeloma in relapse. Lancet 1:926, 1976

1977 49: 379-389

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