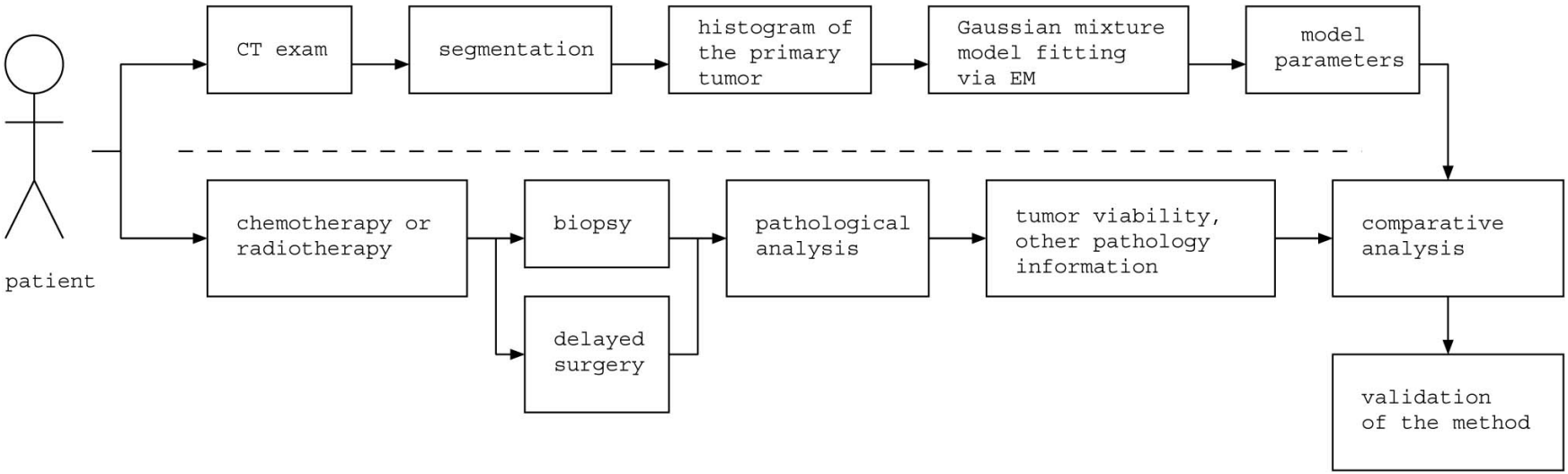
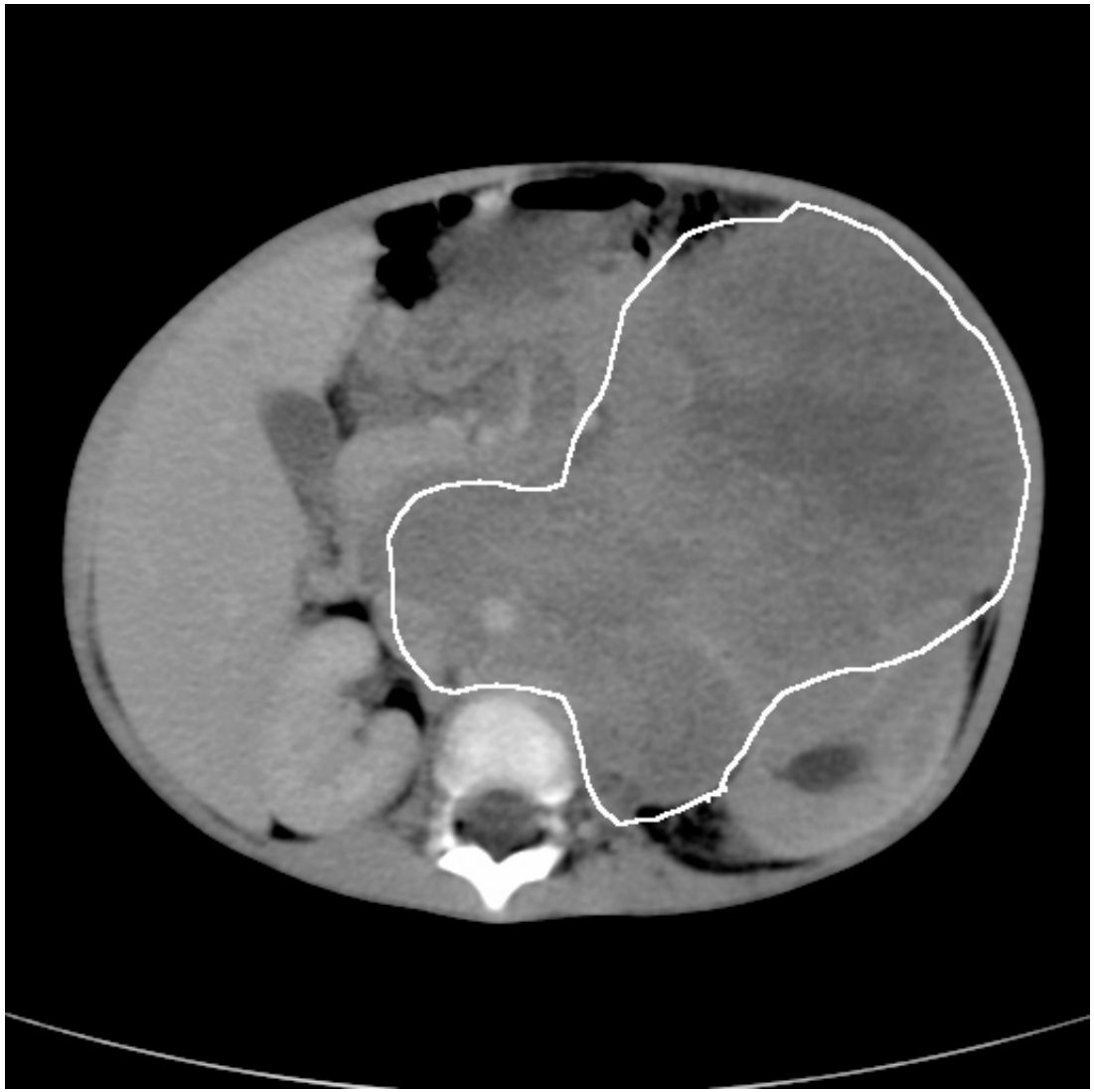
Estimation of the tissue composition of the tumor mass in neuroblastoma

Fábio J. Ayres, Marcelo K. Zuffo,
Rangaraj M. Rangayyan, Graham S. Boag,
Vicente Odone Filho, and Marcelo Valente

University of Calgary, Calgary, AB, Canada
Universidade de São Paulo, São Paulo, SP, Brazil
SENAC College of Computer Science and Technology ,
São Paulo, SP, Brazil
Alberta Children's Hospital, Calgary, AB, Canada
Instituto da Criança, São Paulo, SP, Brazil

Clinical and image-based analysis

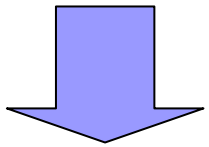




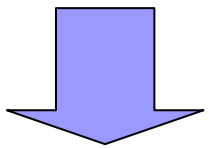
Tumor mass enclosing the aorta, unresectable

Tumor response to therapy

Intermediate density: active or viable tumor



Low density: necrosis



High density: calcified tissue

Gaussian Mixture Model (GMM)

Class probability α_i

Conditional probability of a CT value

$$\mathrm{p}_i\left(x\middle|\mu_i,\sigma_i\right)=\frac{1}{\sigma_i\sqrt{2\pi}}\exp\left(-\frac{\left(x-\mu_i\right)^2}{2\sigma_i}\right)$$

Gaussian Mixture Model

$$\mathrm{p}\left(x\middle|\boldsymbol{\Theta}\right)=\sum_{i=1}^{M}\alpha_i\,\mathrm{p}_i\left(x\middle|\mu_i,\sigma_i\right)$$

$$\boldsymbol{\Theta}=\left(\alpha_1,\mu_1,\sigma_1,\alpha_2,\mu_2,\sigma_2,\ldots,\alpha_M,\mu_M,\sigma_M\right)$$

Maximum-likelihood principle

Likelihood of the parameters (assuming independent samples)

$$\mathrm{L}\left(\boldsymbol{\Theta}\middle|\mathbf{x}\right) \equiv \mathrm{p}\left(\mathbf{x}\middle|\boldsymbol{\Theta}\right) = \prod_{j=1}^{N} \mathrm{p}\left(x_j\middle|\boldsymbol{\Theta}\right)$$

Bayes rule and flat prior assumption

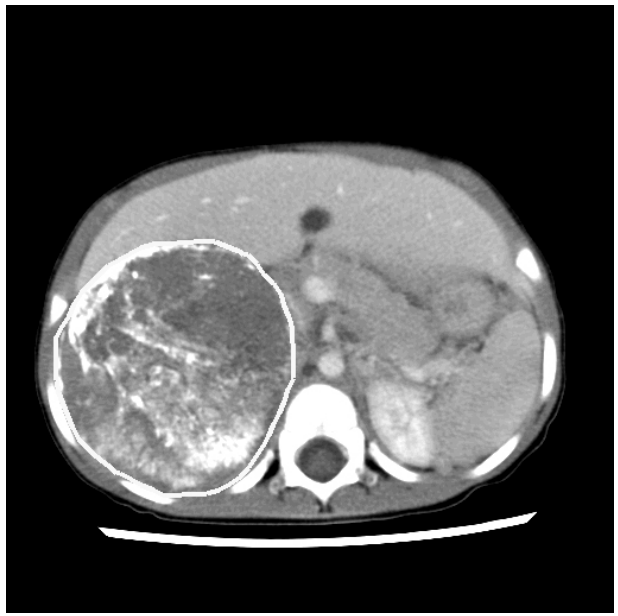
$$\mathrm{p}\left(\boldsymbol{\Theta}\middle|\mathbf{x}\right) = \frac{\mathrm{p}\left(\boldsymbol{\Theta}\right)\mathrm{p}\left(\mathbf{x}\middle|\boldsymbol{\Theta}\right)}{\mathrm{p}\left(\mathbf{x}\right)} \approx \mathrm{L}\left(\boldsymbol{\Theta}\middle|\mathbf{x}\right)$$

$$\boldsymbol{\Theta}_{optimal} = \arg\max_{\boldsymbol{\Theta}} \left\{\mathrm{L}\left(\boldsymbol{\Theta}\middle|\mathbf{x}\right)\right\}$$

Estimation of model parameters

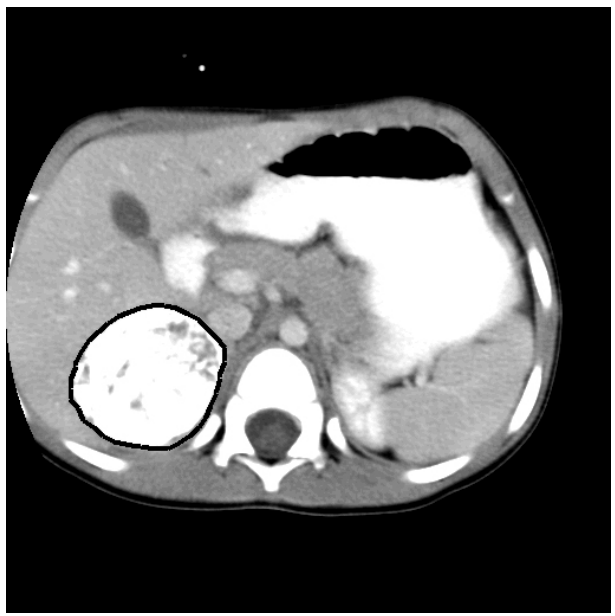
- Assume number of tissue types M=3
- Initialize GMM means to the mean of the tumor histogram and mean ± 0.5 std. dev.
- Initialize GMM variance = variance of the tumor histogram
- Apply Expectation-Maximization algorithm

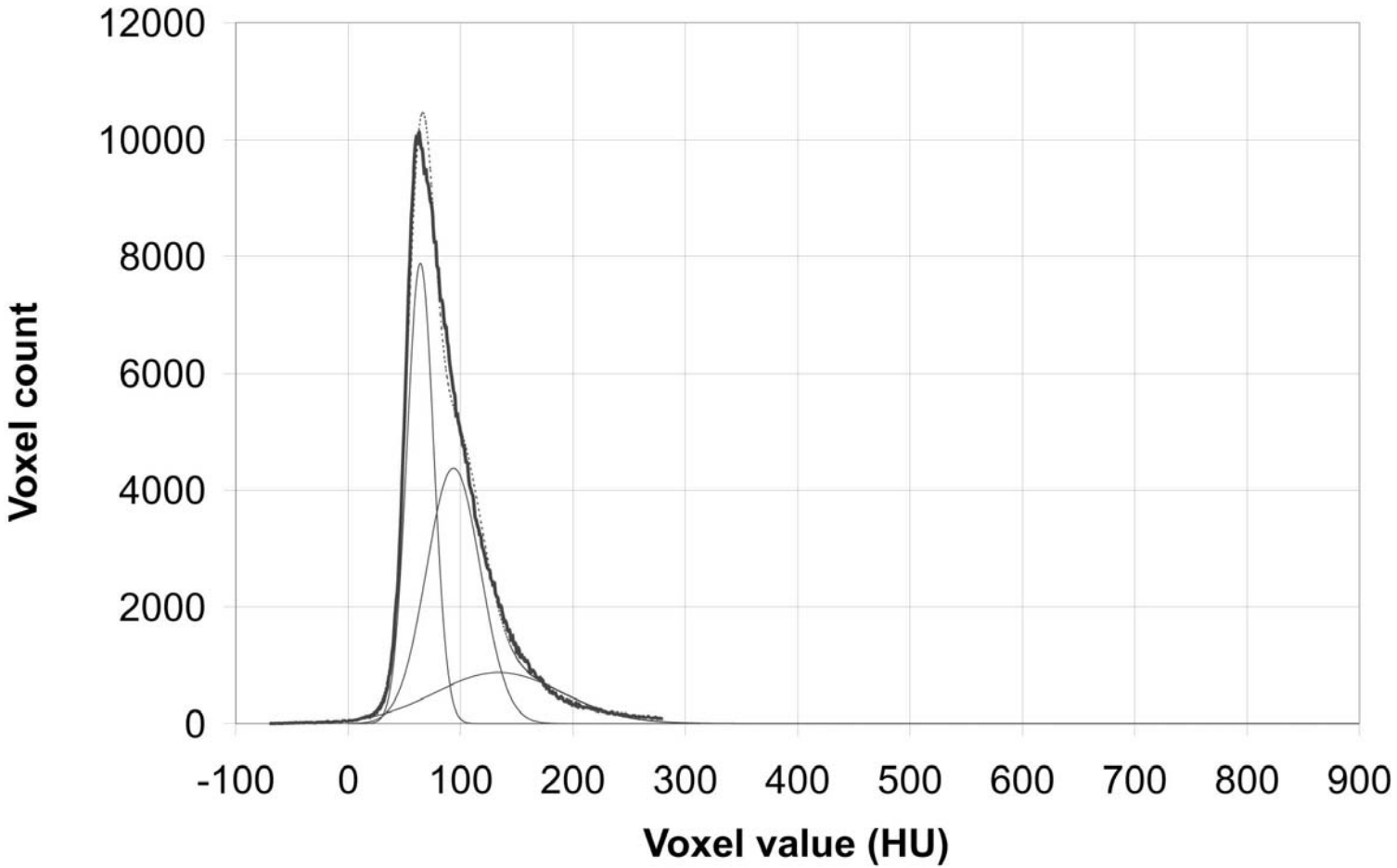
Case 1a
April 2001



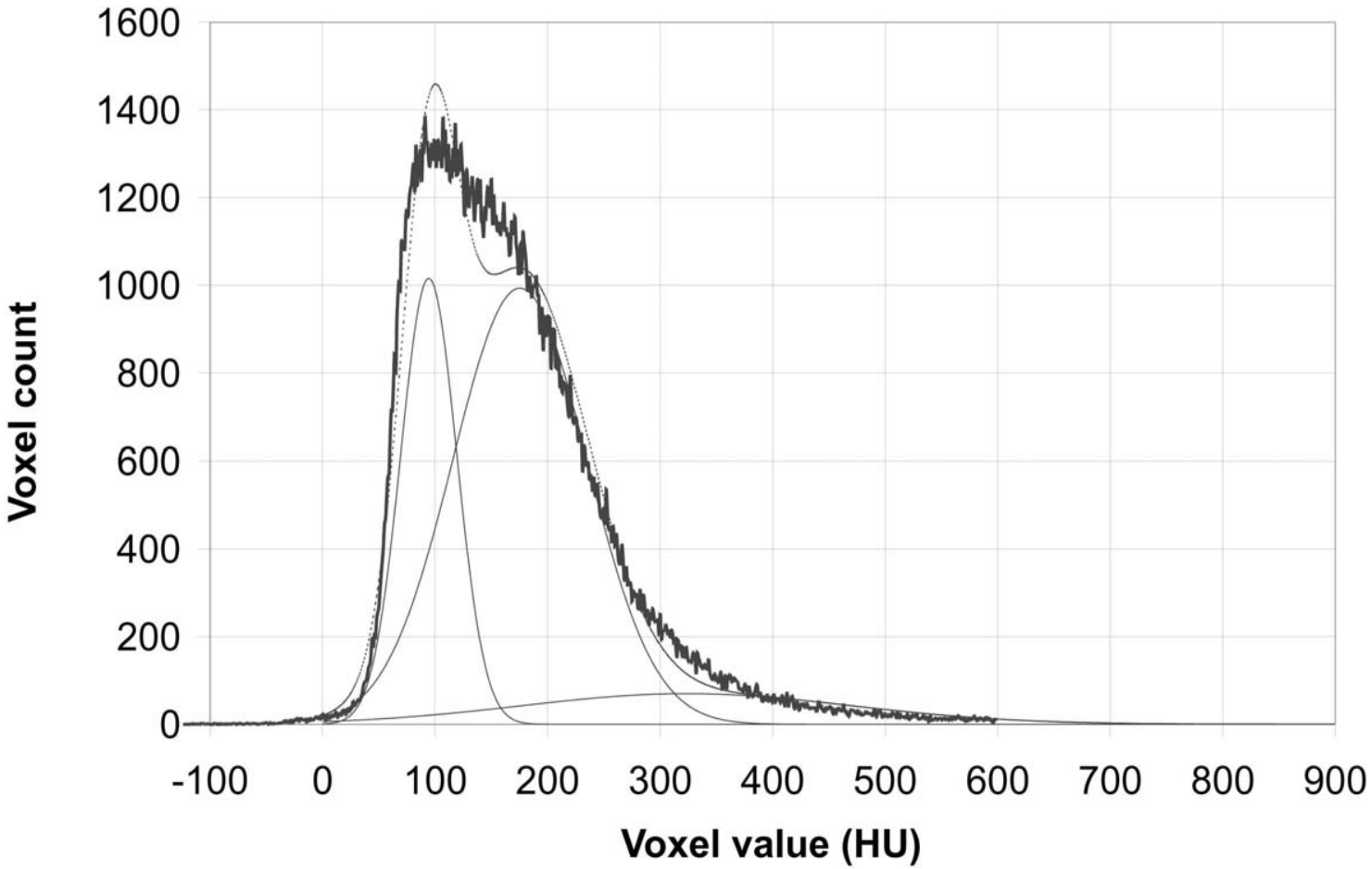
Case 1b
June 2001

Case 1c
Sept 2001

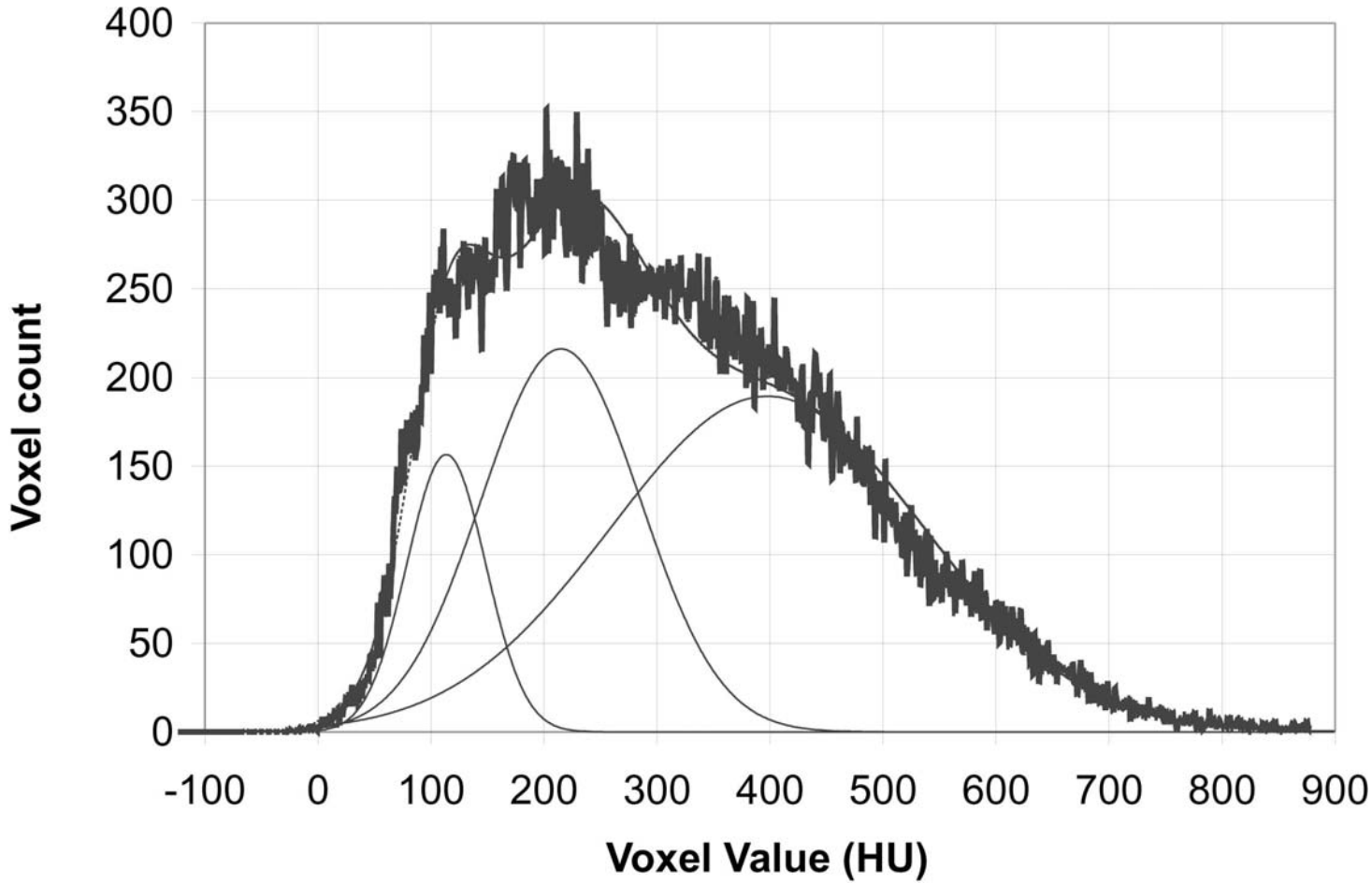




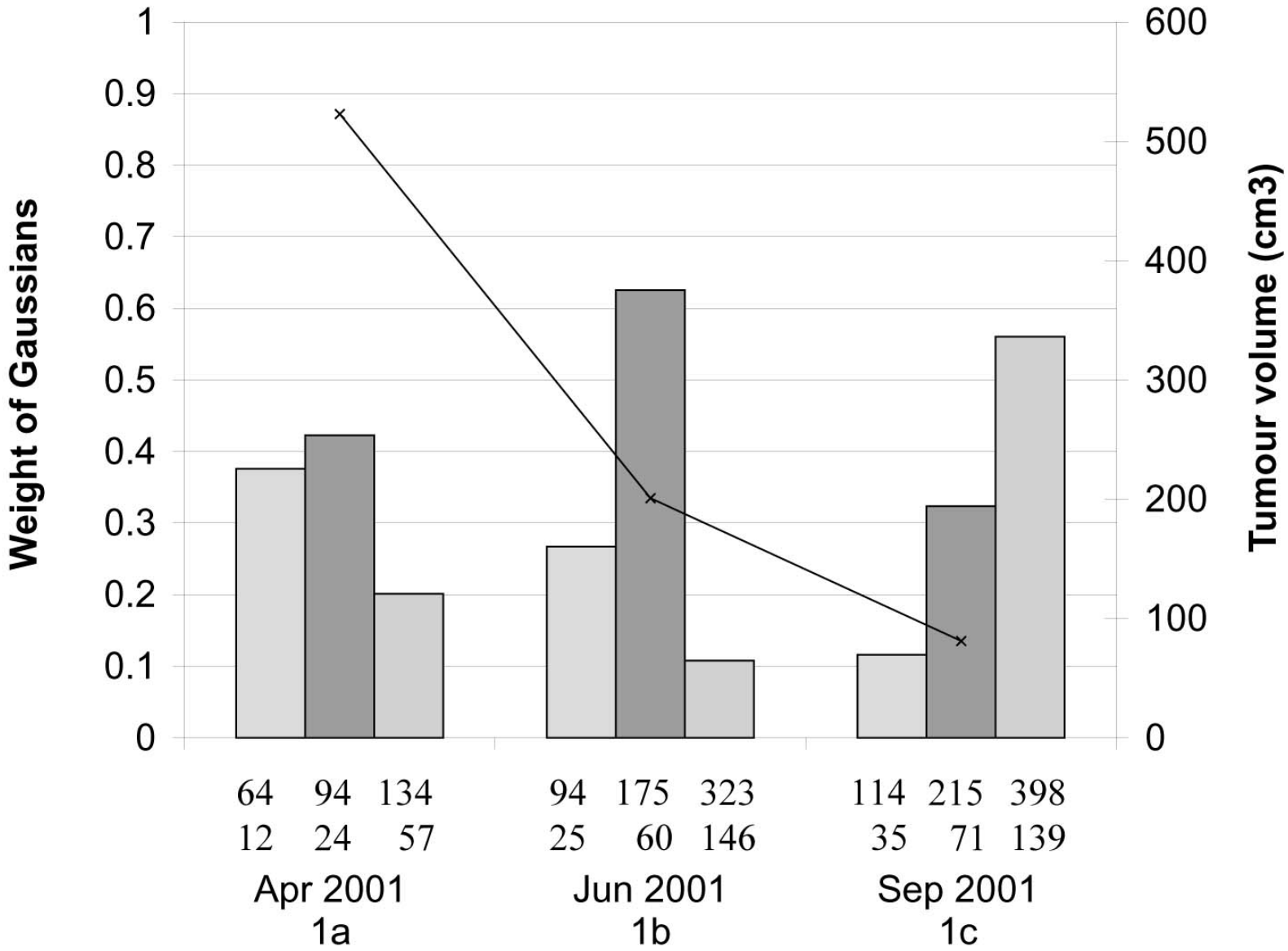
GMM for Case 1a, M = 3



GMM for Case 1b, M = 3

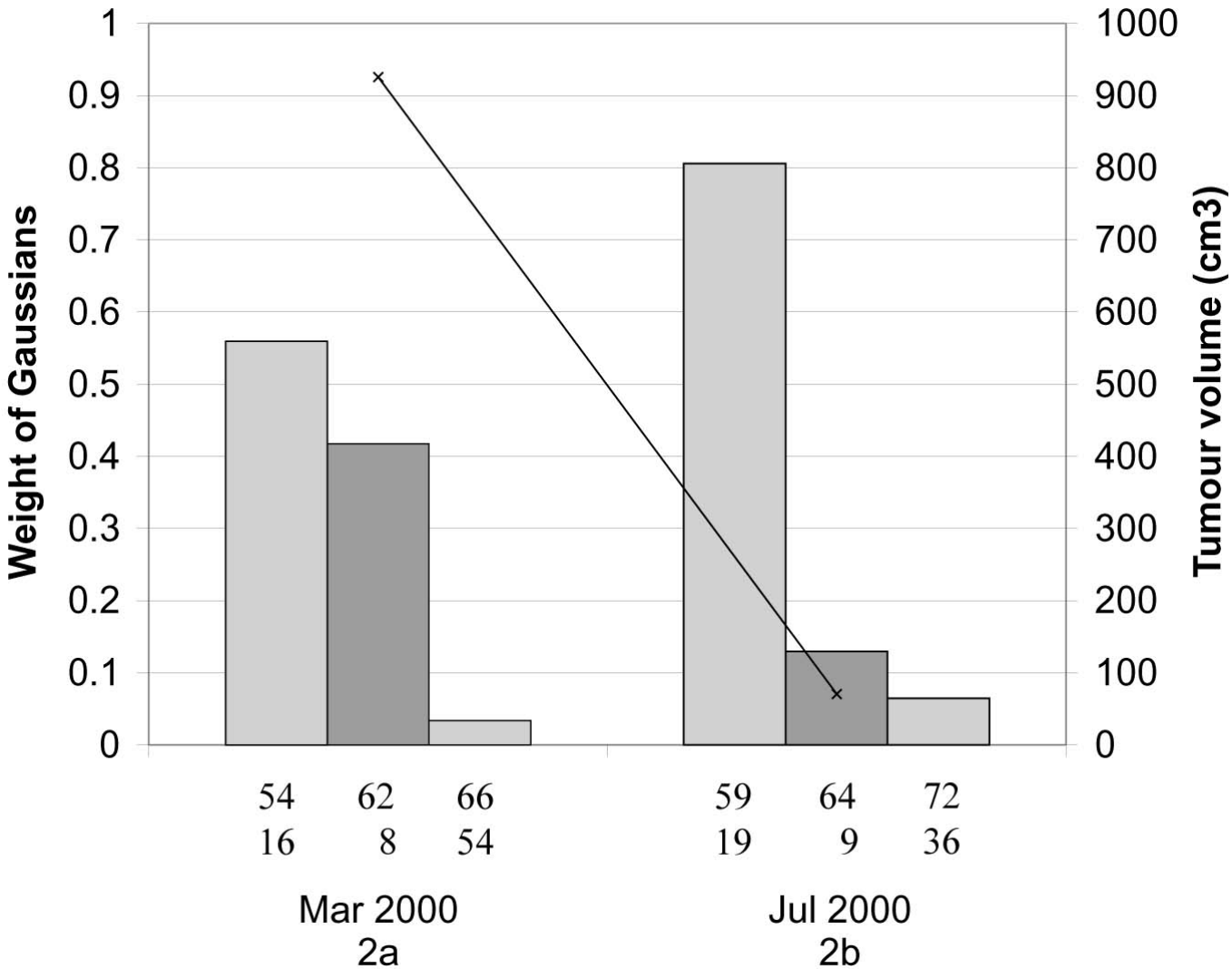


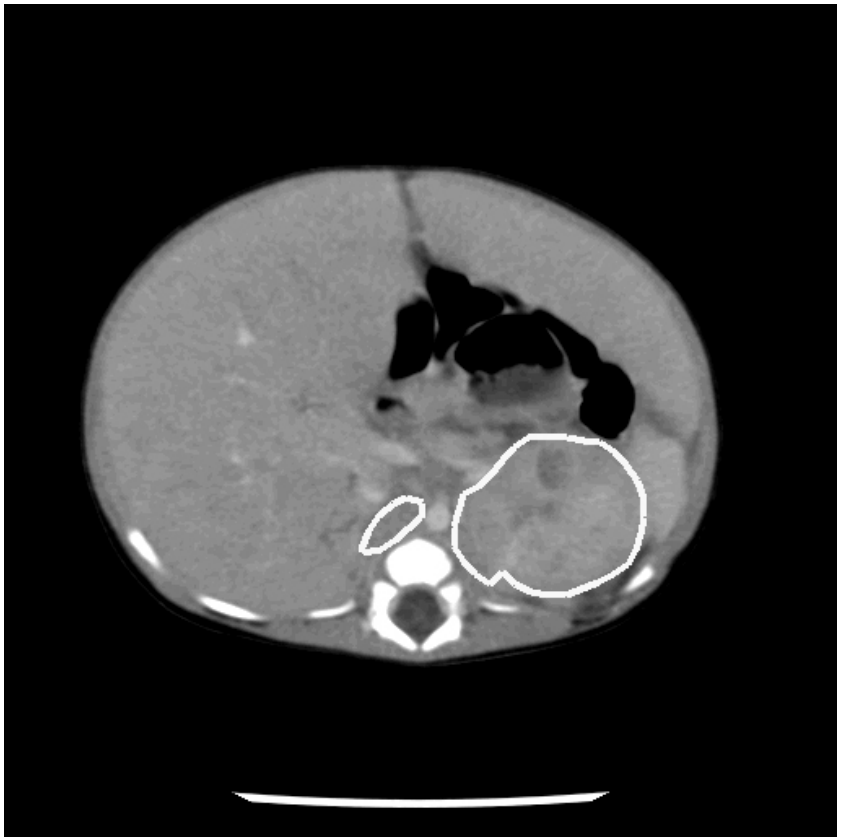
GMM for Case 1c, M = 3


Weight of Gaussians
Tumour volume (cm3)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
600
500
400
300
200
100
0
64 94 134
12 24 57
Apr 2001
1a
94 175 323
25 60 146
Jun 2001
1b
114 215 398
35 71 139
Sep 2001
1c

Case 2a, Mar 2000

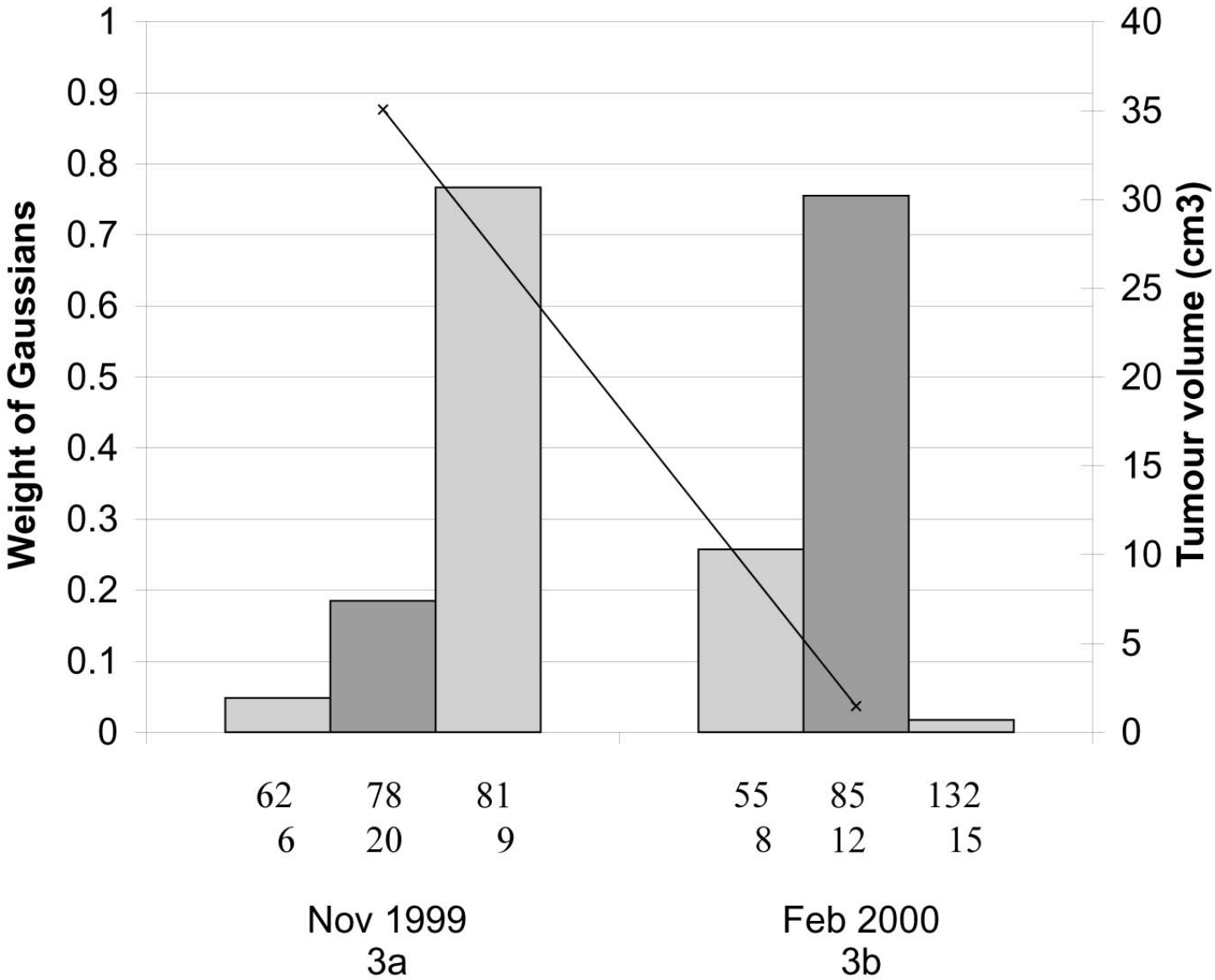
Case 2b, July 2000


Weight of Gaussians
Tumour volume (cm3)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1000
900
800
700
600
500
400
300
200
100
0
54
16
62
8
66
54
59
19
64
9
72
36
Mar 2000
2a
Jul 2000
2b

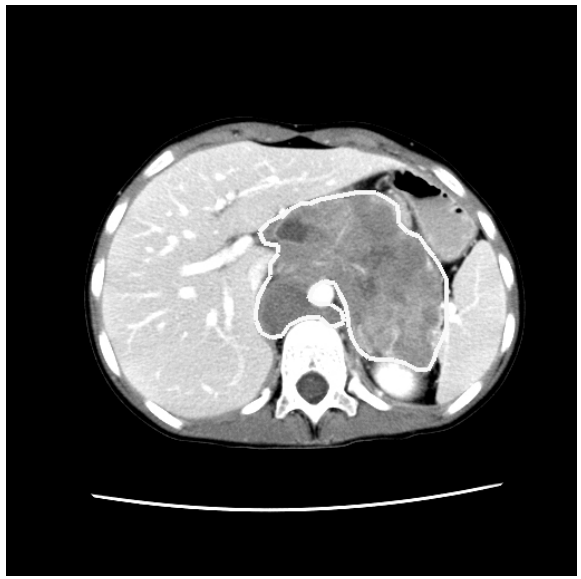


Case 2a, Mar 2000

Case 2b, July 2000

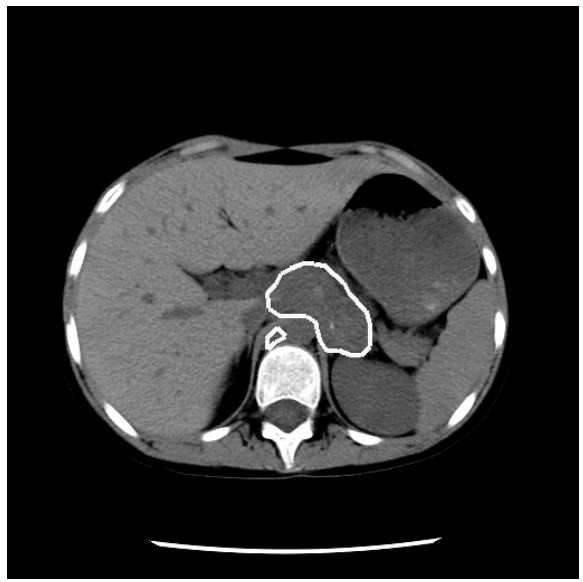

Weight of Gaussians
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Tumour volume (cm3)
40
35
30
25
20
15
10
5
0
62
6
78
20
81
9
55
8
85
12
132
15
Nov 1999
3a
Feb 2000
3b

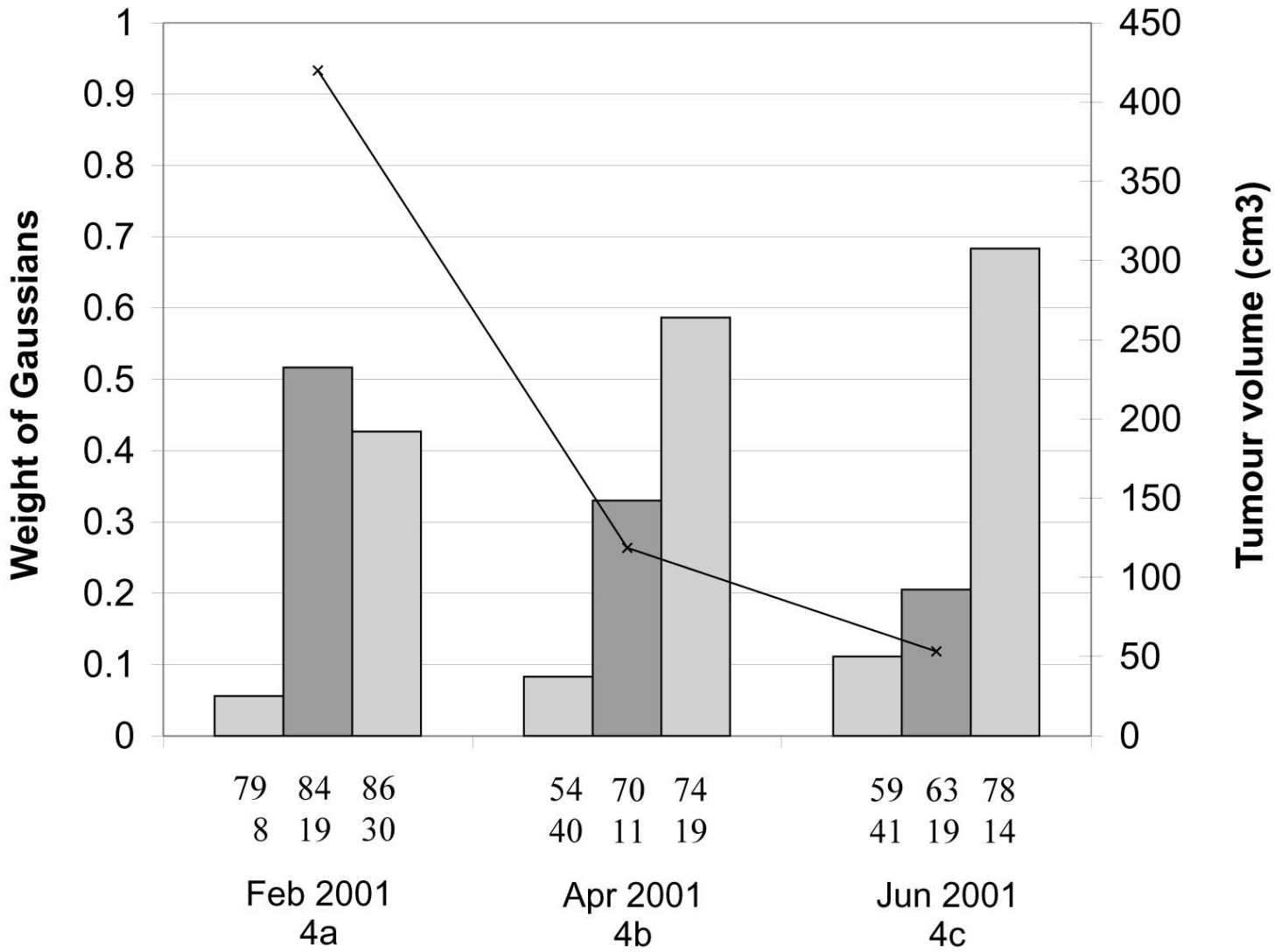
Case 4a
Feb 2001



Case 4b
April 2001

Case 4c
June 2001




Weight of Gaussians
Tumour volume (cm3)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
450
400
350
300
250
200
150
100
50
0
79 84 86
8 19 30
54 70 74
40 11 19
59 63 78
41 19 14
Feb 2001
4a
Apr 2001
4b
Jun 2001
4c

Conclusion

- We have developed a method for objective assessment of tumor response to therapy
- The method provides quantitative parameters representing the tissue composition of the tumor
- The results should assist in planning therapy and delayed surgery

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