

Tumor Size Study: Inter-rater reliability with a fixed second factor*

(1.) Data:

Recall the study designed to determine the reliability of size measurements of tumors in cancer patients, where two researchers recruited 26 oncologists to measure simulated tumors. The simulated tumors were made of one of two materials chosen to physically resemble the texture and size of tumors which are found in cancer patients and they were made in one of three shapes: “small,” “oblong,” and “large”. Two copies of each simulated tumor were made; all were placed randomly in rows on a folded blanket and then covered with a sheet of half-inch foam. The oncologists then independently measured each tumor with their usual equipment (ruler and calipers) and recorded the size obtained. “Size” is “cross-sectional area,” which they define as the product of the longest dimension and the shortest dimension of a tumor. Here we will consider shape and oncologist effects on the size measurement.

Questions: Is there large oncologist-to-oncologist variability in measurement of simulated tumor sizes? Does this vary by tumor shape?

(2.) Exploring the data:

Shown on the following pages are simple statistics and plots exploring means, spread, and normality for these data.

```
DATA onc;
  INFILE "oncology2.dat" FIRSTOBS=2;
  INPUT size oncologist material shape which;
  rep = which + 2*(material EQ 2);
PROC SORT DATA=onc OUT=sorted;
  BY oncologist shape;
RUN;

%INCLUDE "onc.readdata.sas";

ODS SELECT Moments;
RUN;
PROC UNIVARIATE DATA=sorted;
  CLASS shape;
  VAR size;
RUN;
```

*File: ~/Teaching/Anova/TwoWay/Mixed/onc.mixed.tex; last modified March 19, 2007.

```

=====
The UNIVARIATE Procedure
Variable: size
shape = 1

          Moments

N              104    Sum Weights              104
Mean           1000.56731    Sum Observations    104059
Std Deviation  231.658845    Variance      53665.8207
Skewness       0.25507257    Kurtosis      -0.0105451
Uncorrected SS 109645613    Corrected SS   5527579.53
Coeff Variation 23.1527498    Std Error Mean 22.7160187

```

```

=====
The UNIVARIATE Procedure
Variable: size
shape = 2

          Moments

N              104    Sum Weights              104
Mean           1218.11538    Sum Observations    126684
Std Deviation  247.682082    Variance      61346.4137
Skewness       0.51470498    Kurtosis      0.90767221
Uncorrected SS 160634410    Corrected SS   6318680.62
Coeff Variation 20.3332201    Std Error Mean 24.2872263

```

```

=====
The UNIVARIATE Procedure
Variable: size
shape = 3

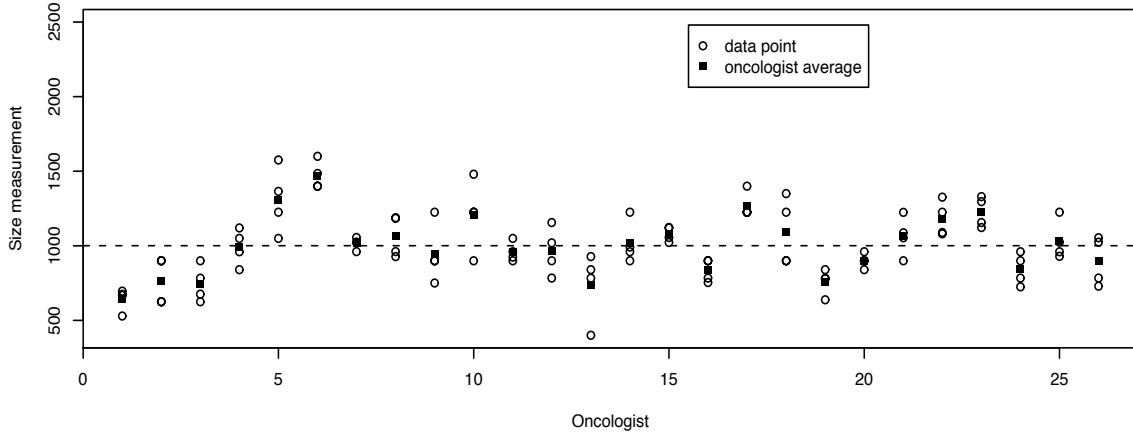
          Moments

N              104    Sum Weights              104
Mean           1485.54808    Sum Observations    154497
Std Deviation  317.407211    Variance      100747.337
Skewness       1.00747702    Kurtosis      1.30404559
Uncorrected SS 239889697    Corrected SS   10376975.8
Coeff Variation 21.3663372    Std Error Mean 31.1243377

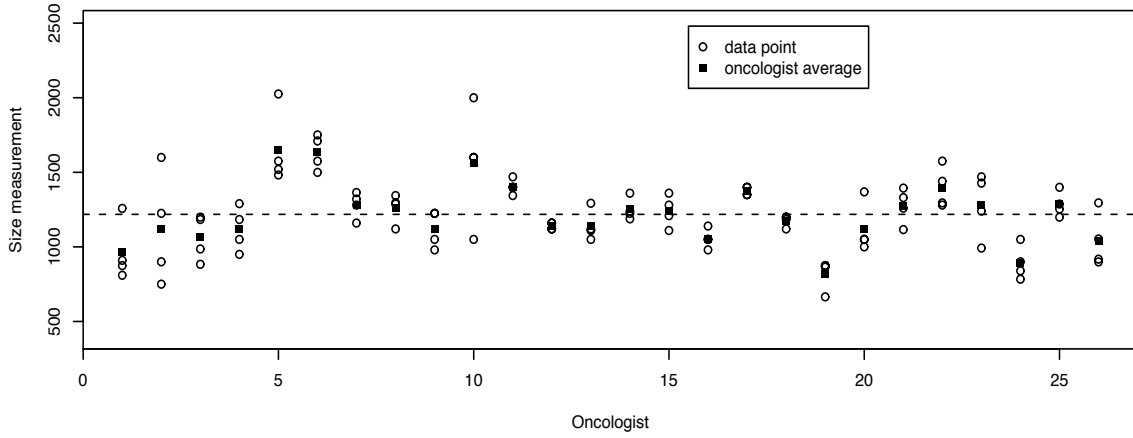
```

Tumor Size Study

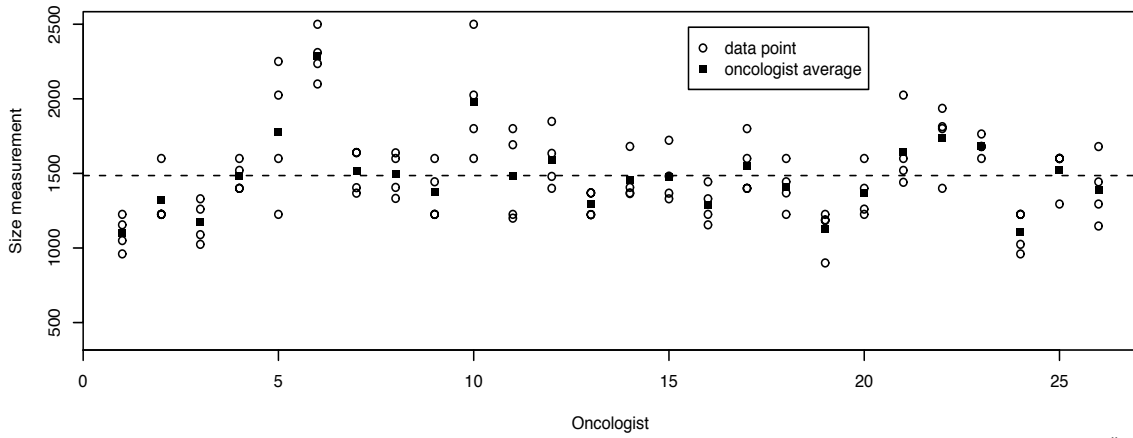
Shape 1 (Small)



Shape 2 (Oblong)

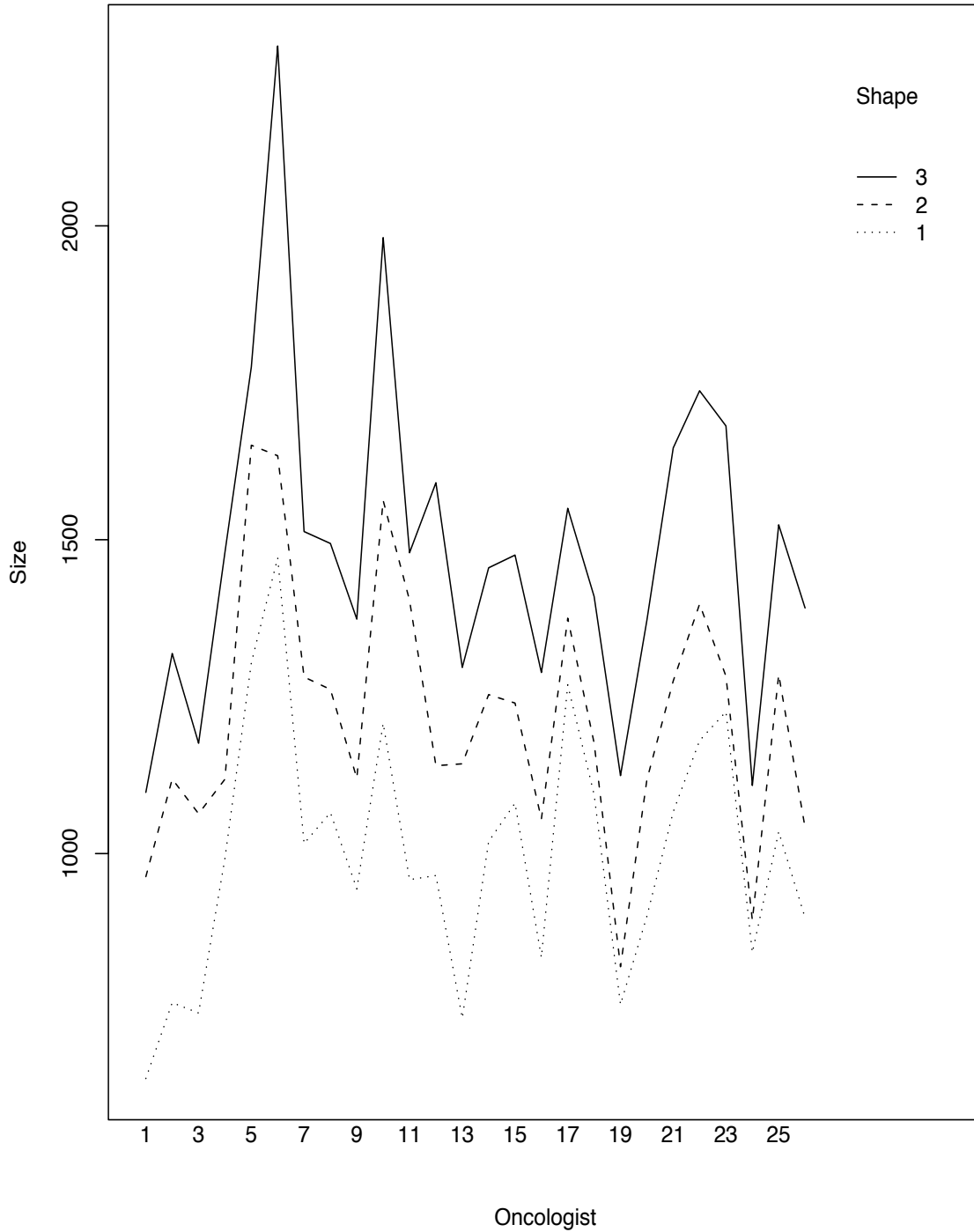


Shape 3 (Large)



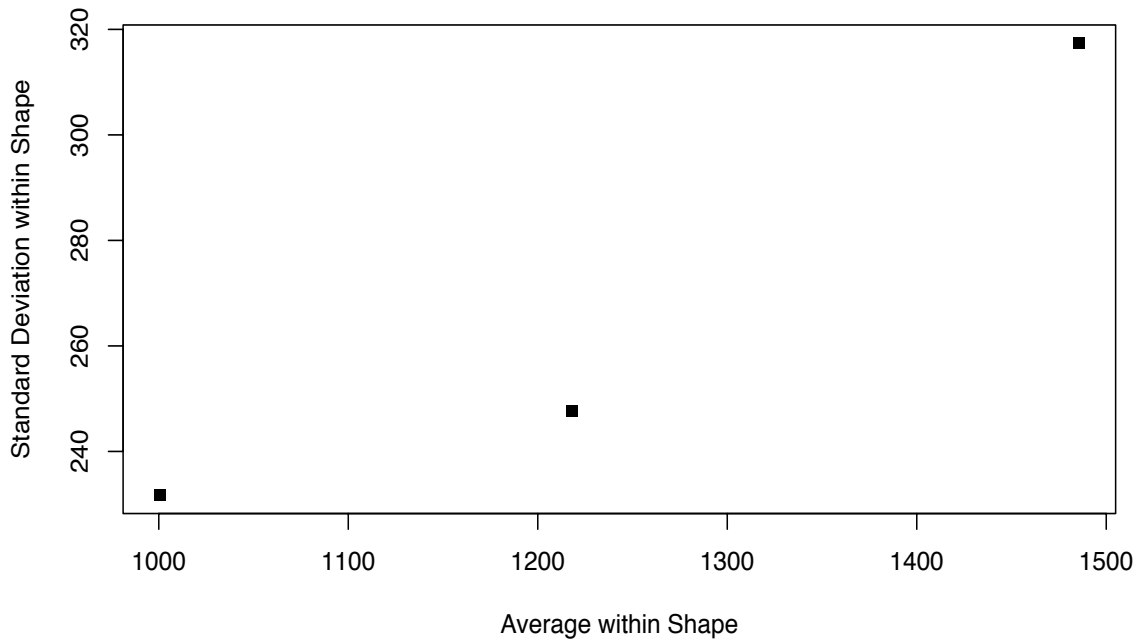
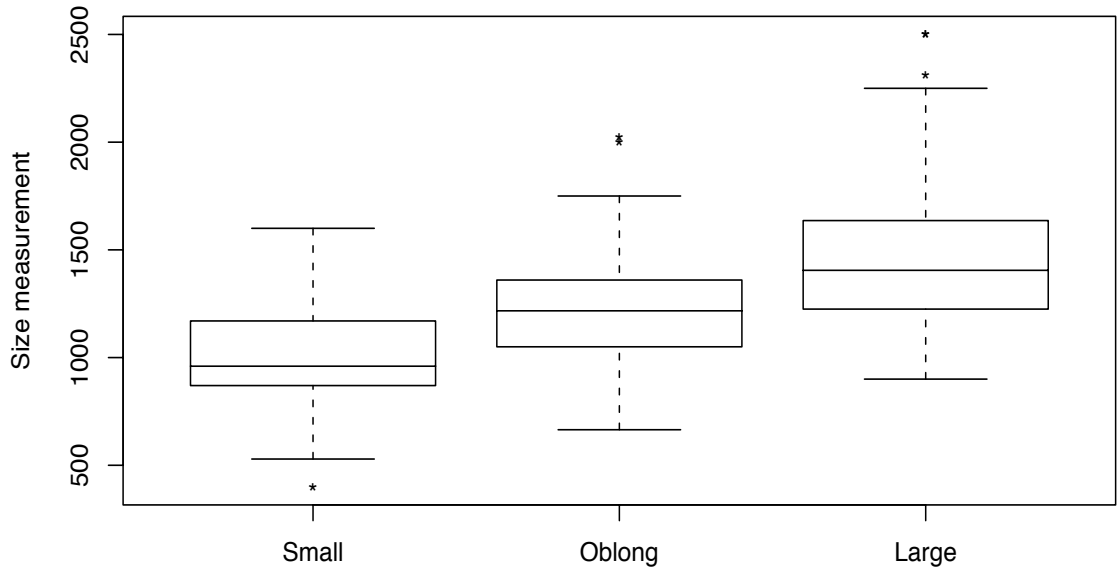
onc.twoway.overall.ps

Tumor Size Study



onc.twoway.interact.ps

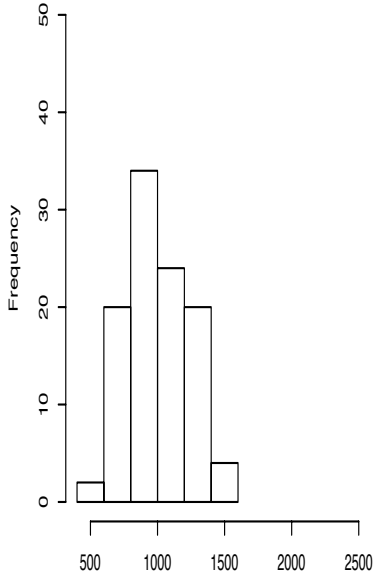
Tumor Size Study



onc.twoway.boxplot.ps

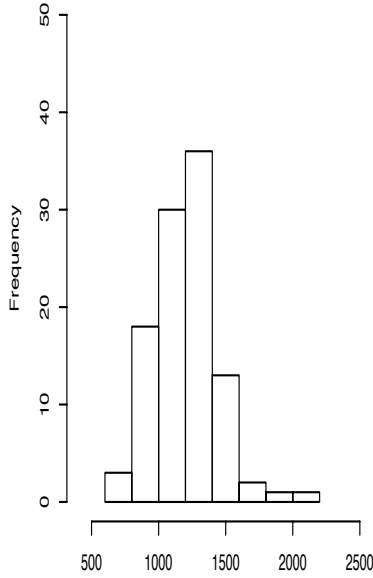
Tumor Size Study

Shape 1 (Small)



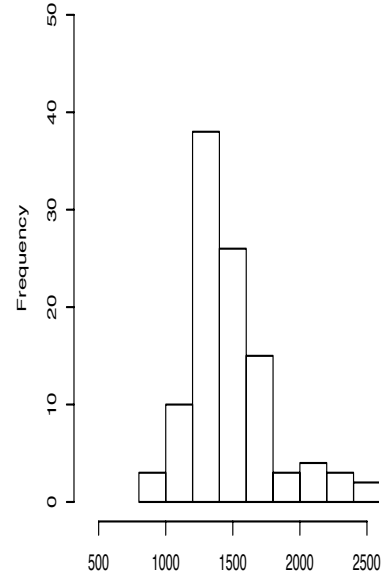
Shape 1 (Small)

Shape 2 (Oblong)

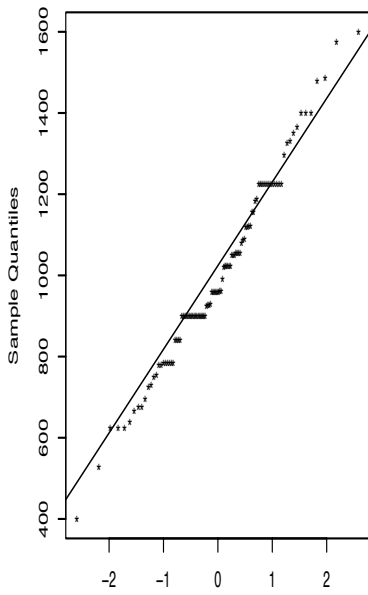


Shape 2 (Oblong)

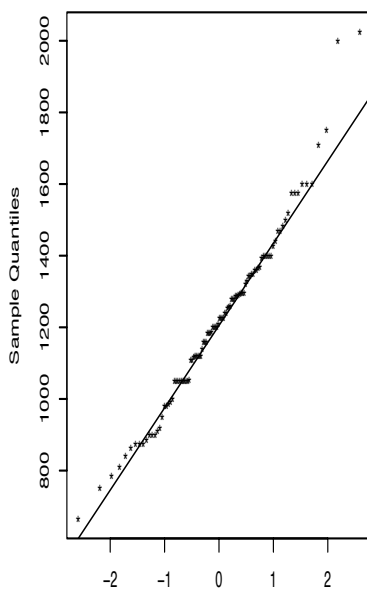
Shape 3 (Large)



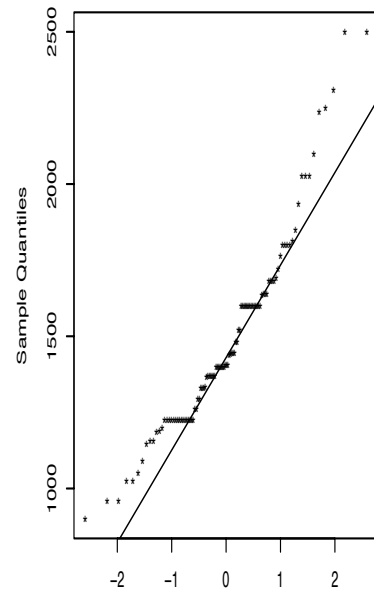
Shape 3 (Large)



Theoretical Quantiles



Theoretical Quantiles



Theoretical Quantiles

onc.twoway.hist.npp.ps

(3.) Two-way mixed effects model:

Since oncologist is a random effect, anything that interacts with oncologist must be a random effect. We will first test whether the oncologist by shape interaction is needed.

```
%INCLUDE "onc.readdata.sas";  
PROC MIXED DATA=sorted METHOD=REML COVTEST;  
  CLASS shape oncologist;  
  MODEL size = shape / SOLUTION;  
  RANDOM INT / SUB=oncologist SOLUTION;  
  RANDOM INT / SUB=shape*oncologist SOLUTION;  
RUN;
```

=====

The SAS System

1

The Mixed Procedure

Model Information

Data Set	WORK.SORTED
Dependent Variable	size
Covariance Structure	Variance Components
Subject Effects	oncologist, shape*oncologist
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	Levels	Values
shape	3	1 2 3
oncologist	26	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

Dimensions

Covariance Parameters	3
Columns in X	4
Columns in Z Per Subject	4
Subjects	26
Max Obs Per Subject	12

Number of Observations

Number of Observations Read	312
Number of Observations Used	312
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	4346.47926086	
1	2	4144.21006267	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
Intercept	oncologist	43716	13061	3.35	0.0004
Intercept	shape*oncologist	0	.	.	.
Residual		29477	2473.65	11.92	<.0001

Fit Statistics

-2 Res Log Likelihood	4144.2
AIC (smaller is better)	4148.2
AICC (smaller is better)	4148.2
BIC (smaller is better)	4150.7

Solution for Fixed Effects

Effect	shape	Estimate	Standard Error	DF	t Value	Pr > t
Intercept		1485.55	44.3262	25	33.51	<.0001
shape	1	-484.98	23.8089	50	-20.37	<.0001
shape	2	-267.43	23.8089	50	-11.23	<.0001
shape	3	0

Solution for Random Effects

Effect	shape	oncologist	Estimate	Std Err Pred	DF	t Value	Pr > t
Intercept		1	-316.15	62.5911	234	-5.05	<.0001
Intercept	1	1	0
Intercept	2	1	0
Intercept	3	1	0
Intercept		2	-159.14	62.5911	234	-2.54	0.0117
Intercept	1	2	0
Intercept	2	2	0
Intercept	3	2	0
Intercept		3	-226.91	62.5911	234	-3.63	0.0004
Intercept	1	3	0
Intercept	2	3	0
Intercept	3	3	0
Intercept		4	-35.7356	62.5911	234	-0.57	0.5686
Intercept	1	4	0
Intercept	2	4	0
Intercept	3	4	0
Intercept		5	323.50	62.5911	234	5.17	<.0001
Intercept	1	5	0
Intercept	2	5	0
Intercept	3	5	0
Intercept		6	532.50	62.5911	234	8.51	<.0001
Intercept	1	6	0
Intercept	2	6	0
Intercept	3	6	0
Intercept		7	33.4596	62.5911	234	0.53	0.5935
Intercept	1	7	0
Intercept	2	7	0
Intercept	3	7	0
Intercept		8	36.7734	62.5911	234	0.59	0.5574
Intercept	1	8	0
Intercept	2	8	0
Intercept	3	8	0
Intercept		9	-84.2590	62.5911	234	-1.35	0.1795
Intercept	1	9	0
Intercept	2	9	0
Intercept	3	9	0
Intercept		10	330.44	62.5911	234	5.28	<.0001
Intercept	1	10	0
Intercept	2	10	0
Intercept	3	10	0
Intercept		11	43.2432	62.5911	234	0.69	0.4903
Intercept	1	11	0
Intercept	2	11	0
Intercept	3	11	0
Intercept		12	-2.6765	62.5911	234	-0.04	0.9659

Intercept	1	12	0
Intercept	2	12	0
Intercept	3	12	0
Intercept	1	13	-166.31	62.5911	234	-2.66	0.0084
Intercept	2	13	0
Intercept	3	13	0
Intercept	1	14	7.4227	62.5911	234	0.12	0.9057
Intercept	2	14	0
Intercept	3	14	0
Intercept	1	15	28.8045	62.5911	234	0.46	0.6458
Intercept	2	15	0
Intercept	3	15	0
Intercept	1	16	-166.08	62.5911	234	-2.65	0.0085
Intercept	2	16	0
Intercept	3	16	0
Intercept	1	17	154.49	62.5911	234	2.47	0.0143
Intercept	2	17	0
Intercept	3	17	0
Intercept	1	18	-7.8839	62.5911	234	-0.13	0.8999
Intercept	2	18	0
Intercept	3	18	0
Intercept	1	19	-315.83	62.5911	234	-5.05	<.0001
Intercept	2	19	0
Intercept	3	19	0
Intercept	1	20	-99.6445	62.5911	234	-1.59	0.1127
Intercept	2	20	0
Intercept	3	20	0
Intercept	1	21	89.4786	62.5911	234	1.43	0.1542
Intercept	2	21	0
Intercept	3	21	0
Intercept	1	22	192.68	62.5911	234	3.08	0.0023
Intercept	2	22	0
Intercept	3	22	0
Intercept	1	23	153.23	62.5911	234	2.45	0.0151
Intercept	2	23	0
Intercept	3	23	0
Intercept	1	24	-271.41	62.5911	234	-4.34	<.0001
Intercept	2	24	0
Intercept	3	24	0
Intercept	1	25	44.0322	62.5911	234	0.70	0.4825
Intercept	2	25	0
Intercept	3	25	0
Intercept	1	26	-118.03	62.5911	234	-1.89	0.0606
Intercept	2	26	0
Intercept	3	26	0

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
shape	2	50	208.19	<.0001

Likelihood ratio tests for models with multiple random effects (intercept random effects like we have here) are not yet established. An approximate Z-test can be carried out. Because it is based on assuming the estimated variance component is normally distributed, the approximation will be

better for larger variance components based on larger sample sizes, but could be quite poor for either smaller variance components or smaller sample sizes.

IMPORTANT NOTE: The log file contains this message: “NOTE: Estimated G matrix is not positive definite.” which the listing file does not contain! Always scan your log file. The G matrix is the variance matrix for the random effects. Variance matrices should always be positive definite, so this is telling you that the model is too complex for these data. We need to re-fit it without the interaction.

```

%INCLUDE "onc.readdata.sas";

PROC MIXED DATA=sorted METHOD=REML COVTEST;
  CLASS shape oncologist;
  MODEL size = shape / SOLUTION;
  RANDOM INT / SUB=oncologist SOLUTION;
RUN;
PROC MIXED DATA=sorted METHOD=REML COVTEST;
  CLASS shape oncologist;
  MODEL size = shape / SOLUTION;
RUN;

=====
The Mixed Procedure

                Model Information

Data Set                WORK.SORTED
Dependent Variable      size
Covariance Structure    Variance Components
Subject Effect          oncologist
Estimation Method       REML
Residual Variance Method Profile
Fixed Effects SE Method Model-Based
Degrees of Freedom Method Containment

                Class Level Information

Class      Levels  Values
shape      3       1 2 3
oncologist 26      1 2 3 4 5 6 7 8 9 10 11 12 13
                14 15 16 17 18 19 20 21 22 23
                24 25 26

                Dimensions
Covariance Parameters    2
Columns in X              4
Columns in Z Per Subject 1
Subjects                  26
Max Obs Per Subject       12

                Number of Observations
Number of Observations Read    312
Number of Observations Used    312
Number of Observations Not Used 0

                Iteration History

Iteration  Evaluations  -2 Res Log Like  Criterion
0          1           4346.47926086
1          1           4144.21006267  0.00000000

                Convergence criteria met.

                Covariance Parameter Estimates

Cov Parm  Subject  Estimate  Standard Error  Z Value  Pr > Z
Intercept oncologist 43716     13061         3.35     0.0004
Residual  29477     2473.64     11.92     <.0001

```

```

Fit Statistics
-2 Res Log Likelihood      4144.2
AIC (smaller is better)   4148.2
AICC (smaller is better)  4148.2
BIC (smaller is better)   4150.7

```

Solution for Fixed Effects

Effect	shape	Estimate	Standard Error	DF	t Value	Pr > t
Intercept		1485.55	44.3264	25	33.51	<.0001
shape	1	-484.98	23.8089	284	-20.37	<.0001
shape	2	-267.43	23.8089	284	-11.23	<.0001
shape	3	0

Solution for Random Effects

Effect	oncologist	Estimate	Std Err	DF	t Value	Pr > t
Intercept	1	-316.15	62.5913	284	-5.05	<.0001
Intercept	2	-159.14	62.5913	284	-2.54	0.0115
Intercept	3	-226.91	62.5913	284	-3.63	0.0003
Intercept	4	-35.7356	62.5913	284	-0.57	0.5685
Intercept	5	323.50	62.5913	284	5.17	<.0001
Intercept	6	532.50	62.5913	284	8.51	<.0001
Intercept	7	33.4597	62.5913	284	0.53	0.5934
Intercept	8	36.7735	62.5913	284	0.59	0.5573
Intercept	9	-84.2591	62.5913	284	-1.35	0.1793
Intercept	10	330.44	62.5913	284	5.28	<.0001
Intercept	11	43.2432	62.5913	284	0.69	0.4902
Intercept	12	-2.6765	62.5913	284	-0.04	0.9659
Intercept	13	-166.32	62.5913	284	-2.66	0.0083
Intercept	14	7.4227	62.5913	284	0.12	0.9057
Intercept	15	28.8046	62.5913	284	0.46	0.6457
Intercept	16	-166.08	62.5913	284	-2.65	0.0084
Intercept	17	154.49	62.5913	284	2.47	0.0142
Intercept	18	-7.8839	62.5913	284	-0.13	0.8999
Intercept	19	-315.83	62.5913	284	-5.05	<.0001
Intercept	20	-99.6446	62.5913	284	-1.59	0.1125
Intercept	21	89.4786	62.5913	284	1.43	0.1539
Intercept	22	192.68	62.5913	284	3.08	0.0023
Intercept	23	153.23	62.5913	284	2.45	0.0150
Intercept	24	-271.41	62.5913	284	-4.34	<.0001
Intercept	25	44.0322	62.5913	284	0.70	0.4823
Intercept	26	-118.03	62.5913	284	-1.89	0.0604

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
shape	2	284	208.19	<.0001

=====

The Mixed Procedure

Model Information

```

Data Set                WORK.SORTED
Dependent Variable      size
Covariance Structure    Diagonal
Estimation Method       REML
Residual Variance Method Profile
Fixed Effects SE Method Model-Based
Degrees of Freedom Method Residual

```

Class Level Information

Class	Levels	Values
shape	3	1 2 3
oncologist	26	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

Dimensions

```

Covariance Parameters    1
Columns in X             4

```

```

Columns in Z          0
Subjects              1
Max Obs Per Subject  312

```

```

Number of Observations
Number of Observations Read  312
Number of Observations Used  312
Number of Observations Not Used  0

```

Covariance Parameter Estimates

Cov Parm	Estimate	Standard Error	Z Value	Pr Z
Residual	71920	5786.08	12.43	<.0001

Fit Statistics

```

-2 Res Log Likelihood  4346.5
AIC (smaller is better)  4348.5
AICC (smaller is better)  4348.5
BIC (smaller is better)  4352.2

```

Solution for Fixed Effects

Effect	shape	Estimate	Standard Error	DF	t Value	Pr > t
Intercept		1485.55	26.2971	309	56.49	<.0001
shape	1	-484.98	37.1897	309	-13.04	<.0001
shape	2	-267.43	37.1897	309	-7.19	<.0001
shape	3	0

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr >
shape	2	309	85.33	<.0001

Does a likelihood ratio test for the oncologist-to-oncologist variability give you a different answer than the Z-test?

Report the results of this study in language a non-statistician could understand.

(4.) Diagnostics:

We examine the same types of plots and statistics for diagnosing mixed models that we did for the one-way and two-way random models. Is there any evidence that model assumptions were violated?

```
%INCLUDE "onc.readdata.sas";

ODS LISTING CLOSE;
RUN;
PROC MIXED DATA=sorted METHOD=REML;
  CLASS shape oncologist;
  MODEL size = shape / OUP = csfits;
  RANDOM INT / SUB = oncologist;
RUN;
ODS LISTING;
RUN;
DATA csfits;
  SET csfits;
  KEEP size shape oncologist rep Pred Resid;
PROC PRINT DATA=csfits;
  WHERE oncologist LE 2;
  TITLE "PARTIAL LISTING OF DIAGNOSTIC DATA SET csfits";
DATA _NULL_;
  SET csfits;
  FILE "onc.diag.dat";
  IF _N_ = 1 THEN PUT "size shape oncologist rep Pred Resid";
  PUT size shape oncologist rep Pred Resid;
RUN;

ODS LISTING CLOSE;
ODS OUTPUT SolutionR = ranfits;
PROC MIXED DATA=sorted METHOD=REML;
  CLASS shape oncologist;
  MODEL size = shape;
  RANDOM INT / SUB=oncologist SOLUTION;
RUN;
ODS OUTPUT CLOSE;
ODS LISTING;
PROC PRINT DATA=ranfits;
  TITLE "COMPLETE RANDOM EFFECTS DATA SET ranfits";
RUN;
DATA _NULL_;
  SET ranfits;
  FILE "onc.ranfits.dat";
  IF _N_ = 1 THEN PUT "effect oncologist estimate";
  PUT effect oncologist estimate;
RUN;
```

=====

PARTIAL LISTING OF DIAGNOSTIC DATA SET csfits

1

Obs	size	oncologist	shape	rep	Pred	Resid
1	667	1	1	1	684.42	-17.421
2	529	1	1	2	684.42	-155.421
3	696	1	1	3	684.42	11.579
4	675	1	1	4	684.42	-9.421
5	1258	1	2	1	901.97	356.031
6	810	1	2	2	901.97	-91.969
7	875	1	2	3	901.97	-26.969
8	910	1	2	4	901.97	8.031
9	1050	1	3	1	1169.40	-119.402
10	960	1	3	2	1169.40	-209.402
11	1225	1	3	3	1169.40	55.598
12	1155	1	3	4	1169.40	-14.402
13	625	2	1	1	841.43	-216.432
14	900	2	1	2	841.43	58.568
15	625	2	1	3	841.43	-216.432
16	900	2	1	4	841.43	58.568
17	750	2	2	1	1058.98	-308.980
18	1225	2	2	2	1058.98	166.020

19	900	2	2	3	1058.98	-158.980
20	1600	2	2	4	1058.98	541.020
21	1225	2	3	1	1326.41	-101.413
22	1225	2	3	2	1326.41	-101.413
23	1225	2	3	3	1326.41	-101.413
24	1600	2	3	4	1326.41	273.587

=====

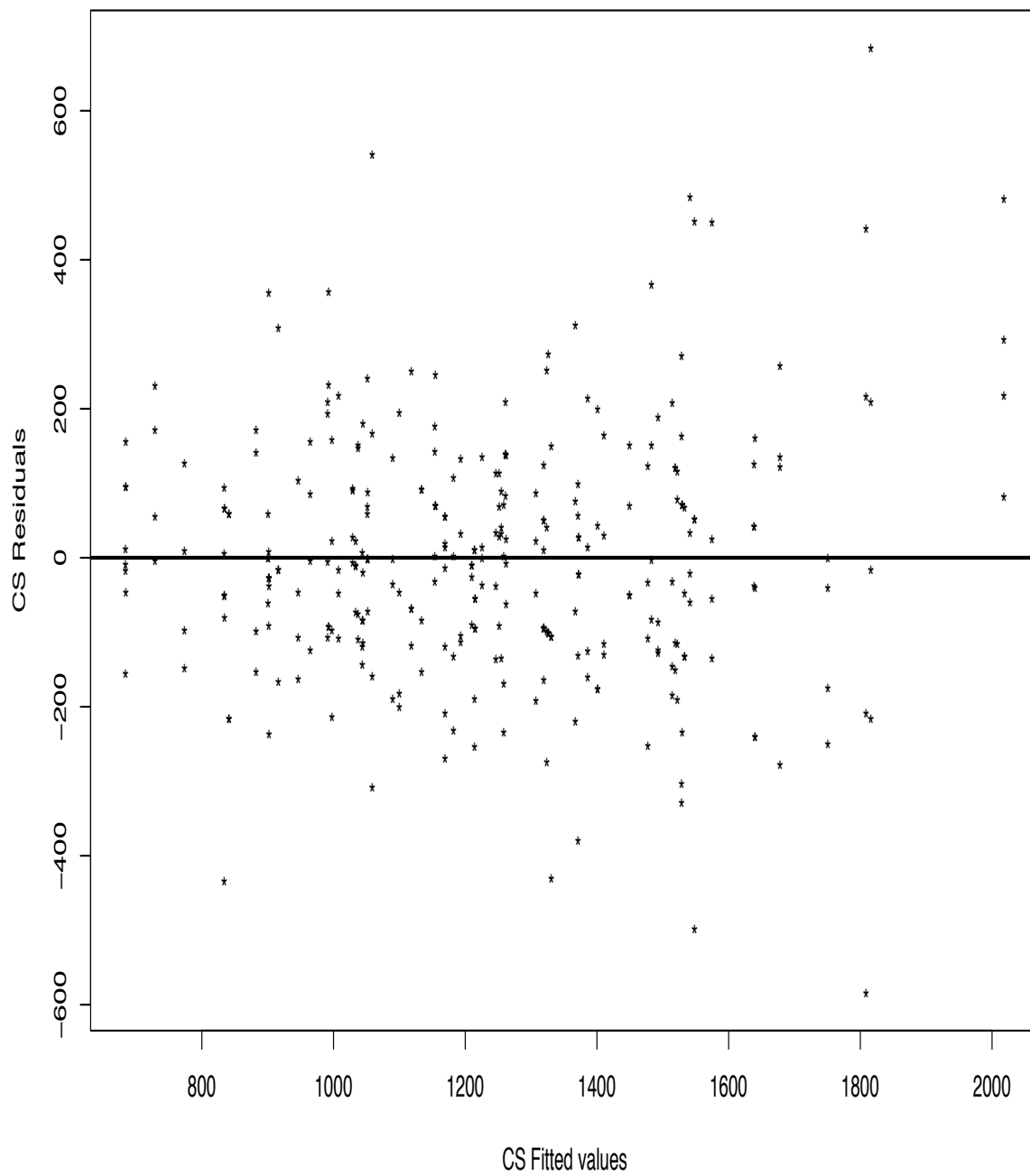
COMPLETE RANDOM EFFECTS DATA SET ranfits

2

Obs	Effect	oncologist	Estimate	StdErr Pred	DF	tValue	Probt
1	Intercept	1	-316.15	62.5913	284	-5.05	<.0001
2	Intercept	2	-159.14	62.5913	284	-2.54	0.0115
3	Intercept	3	-226.91	62.5913	284	-3.63	0.0003
4	Intercept	4	-35.7356	62.5913	284	-0.57	0.5685
5	Intercept	5	323.50	62.5913	284	5.17	<.0001
6	Intercept	6	532.50	62.5913	284	8.51	<.0001
7	Intercept	7	33.4597	62.5913	284	0.53	0.5934
8	Intercept	8	36.7735	62.5913	284	0.59	0.5573
9	Intercept	9	-84.2591	62.5913	284	-1.35	0.1793
10	Intercept	10	330.44	62.5913	284	5.28	<.0001
11	Intercept	11	43.2432	62.5913	284	0.69	0.4902
12	Intercept	12	-2.6765	62.5913	284	-0.04	0.9659
13	Intercept	13	-166.32	62.5913	284	-2.66	0.0083
14	Intercept	14	7.4227	62.5913	284	0.12	0.9057
15	Intercept	15	28.8046	62.5913	284	0.46	0.6457
16	Intercept	16	-166.08	62.5913	284	-2.65	0.0084
17	Intercept	17	154.49	62.5913	284	2.47	0.0142
18	Intercept	18	-7.8839	62.5913	284	-0.13	0.8999
19	Intercept	19	-315.83	62.5913	284	-5.05	<.0001
20	Intercept	20	-99.6446	62.5913	284	-1.59	0.1125
21	Intercept	21	89.4786	62.5913	284	1.43	0.1539
22	Intercept	22	192.68	62.5913	284	3.08	0.0023
23	Intercept	23	153.23	62.5913	284	2.45	0.0150
24	Intercept	24	-271.41	62.5913	284	-4.34	<.0001
25	Intercept	25	44.0322	62.5913	284	0.70	0.4823
26	Intercept	26	-118.03	62.5913	284	-1.89	0.0604

Tumor Size Study

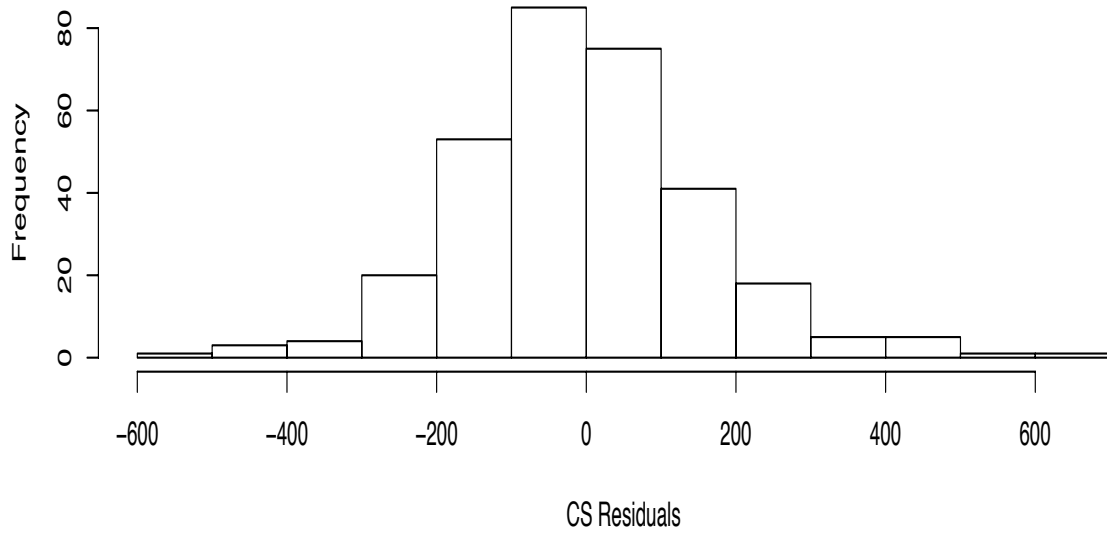
CS residuals vs. CS fitted values



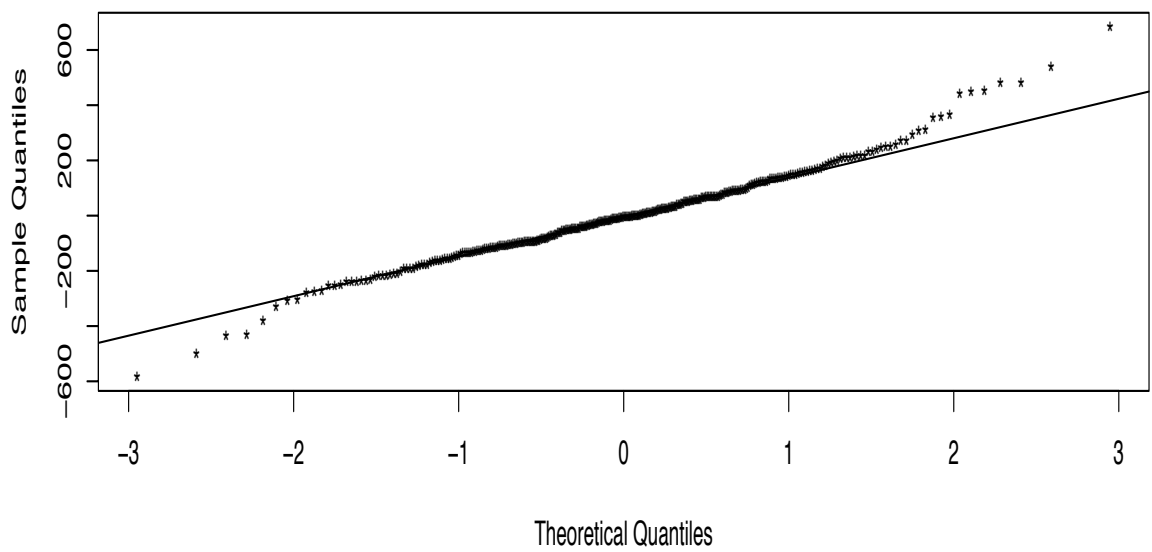
onc.twoway.res.fits.ps

Tumor Size Study

Histograms of CS residuals



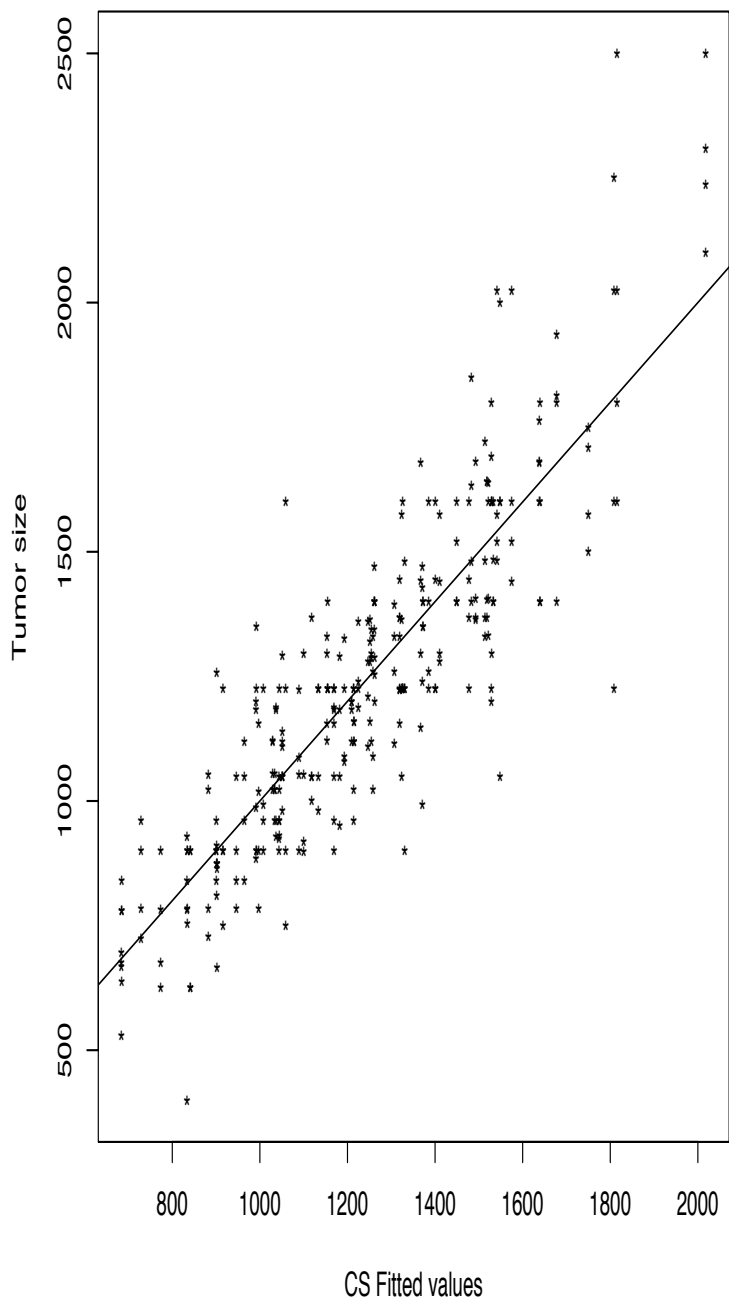
CS Residuals



onc.twoway.res.hist.npp.ps

Tumor Size Study

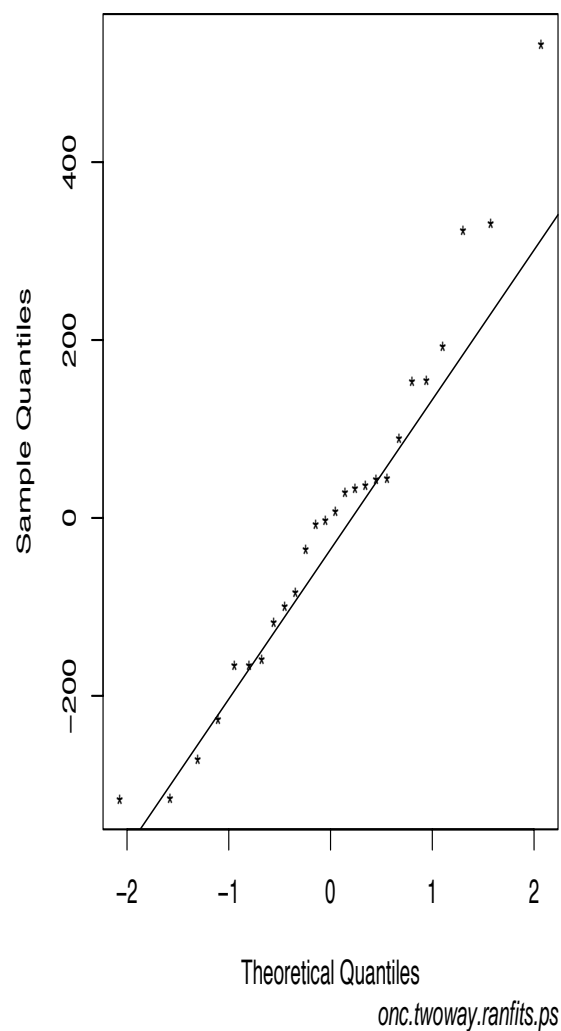
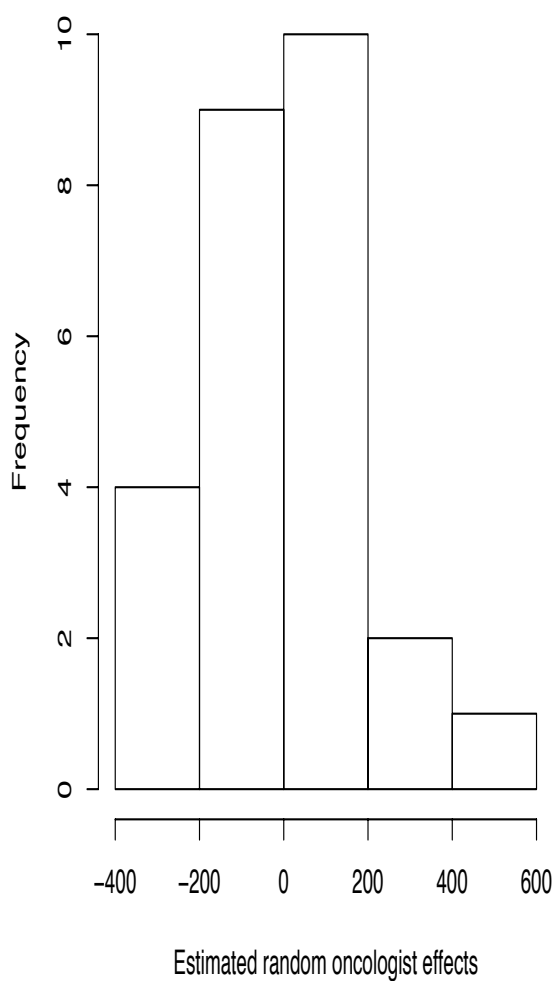
Observed vs. CS fitted values



onc.twoway.obs.fits.ps

Tumor Size Study

Histograms and quantile plots of estimated random effects



onc.twoway.ranfits.ps

(5.) Fitting the model in PROC GLM:

Compare the results below to those from PROC MIXED with the interaction. Are the estimated variance components different? Is the test of the shape main effect different? Are the estimated random effects different?

```
%INCLUDE "onc.readdata.sas";

PROC GLM DATA=sorted;
  CLASS shape oncologist;
  MODEL size = shape oncologist shape*oncologist / SOLUTION;
  RANDOM oncologist shape*oncologist / TEST;
RUN;
```

=====

The SAS System 1

The GLM Procedure

Class Level Information

Class	Levels	Values
shape	3	1 2 3
oncologist	26	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

Number of Observations Read 312
 Number of Observations Used 312

=====

The SAS System 2

The GLM Procedure

Dependent Variable: size

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	77	27575930.49	358128.97	12.11	<.0001
Error	234	6921169.00	29577.65		
Corrected Total	311	34497099.49			

R-Square	Coeff Var	Root MSE	size Mean
0.799370	13.92852	171.9815	1234.744

Source	DF	Type I SS	Mean Square	F Value	Pr > F
shape	2	12273863.58	6136931.79	207.49	<.0001
oncologist	25	13851803.32	554072.13	18.73	<.0001
shape*oncologist	50	1450263.58	29005.27	0.98	0.5162

Source	DF	Type III SS	Mean Square	F Value	Pr > F
shape	2	12273863.58	6136931.79	207.49	<.0001
oncologist	25	13851803.32	554072.13	18.73	<.0001
shape*oncologist	50	1450263.58	29005.27	0.98	0.5162

Parameter	Estimate	Standard Error	t Value	Pr > t
-----------	----------	----------------	---------	---------

Intercept		1391.250000 B	85.9907630	16.18	<.0001
shape	1	-493.500000 B	121.6093033	-4.06	<.0001
shape	2	-350.000000 B	121.6093033	-2.88	0.0044
shape	3	0.000000 B	.	.	.
oncologist	1	-293.750000 B	121.6093033	-2.42	0.0165
oncologist	2	-72.500000 B	121.6093033	-0.60	0.5516
oncologist	3	-215.500000 B	121.6093033	-1.77	0.0777
oncologist	4	88.750000 B	121.6093033	0.73	0.4662
oncologist	5	383.750000 B	121.6093033	3.16	0.0018
oncologist	6	895.250000 B	121.6093033	7.36	<.0001
oncologist	7	121.750000 B	121.6093033	1.00	0.3178
oncologist	8	102.750000 B	121.6093033	0.84	0.3990
oncologist	9	-17.750000 B	121.6093033	-0.15	0.8841
oncologist	10	590.000000 B	121.6093033	4.85	<.0001
oncologist	11	88.000000 B	121.6093033	0.72	0.4700
oncologist	12	199.500000 B	121.6093033	1.64	0.1022
oncologist	13	-94.750000 B	121.6093033	-0.78	0.4367
oncologist	14	64.000000 B	121.6093033	0.53	0.5992
oncologist	15	84.250000 B	121.6093033	0.69	0.4891
oncologist	16	-102.750000 B	121.6093033	-0.84	0.3990
oncologist	17	158.750000 B	121.6093033	1.31	0.1930
oncologist	18	18.250000 B	121.6093033	0.15	0.8808
oncologist	19	-267.000000 B	121.6093033	-2.20	0.0291
oncologist	20	-20.000000 B	121.6093033	-0.16	0.8695
oncologist	21	255.000000 B	121.6093033	2.10	0.0371
oncologist	22	346.000000 B	121.6093033	2.85	0.0048
oncologist	23	290.000000 B	121.6093033	2.38	0.0179
oncologist	24	-282.750000 B	121.6093033	-2.33	0.0209
oncologist	25	132.500000 B	121.6093033	1.09	0.2770
oncologist	26	0.000000 B	.	.	.
shape*oncologist	1 1	37.750000 B	171.9815260	0.22	0.8265
shape*oncologist	1 2	-62.750000 B	171.9815260	-0.36	0.7155
shape*oncologist	1 3	63.750000 B	171.9815260	0.37	0.7112
shape*oncologist	1 4	6.000000 B	171.9815260	0.03	0.9722
shape*oncologist	1 5	22.250000 B	171.9815260	0.13	0.8972
shape*oncologist	1 6	-321.750000 B	171.9815260	-1.87	0.0626
shape*oncologist	1 7	-3.500000 B	171.9815260	-0.02	0.9838
shape*oncologist	1 8	64.750000 B	171.9815260	0.38	0.7069
shape*oncologist	1 9	63.750000 B	171.9815260	0.37	0.7112
shape*oncologist	1 10	-280.250000 B	171.9815260	-1.63	0.1045
shape*oncologist	1 11	-27.250000 B	171.9815260	-0.16	0.8742
shape*oncologist	1 12	-132.250000 B	171.9815260	-0.77	0.4427
shape*oncologist	1 13	-65.250000 B	171.9815260	-0.38	0.7047
shape*oncologist	1 14	57.500000 B	171.9815260	0.33	0.7384
shape*oncologist	1 15	98.250000 B	171.9815260	0.57	0.5684
shape*oncologist	1 16	39.500000 B	171.9815260	0.23	0.8185
shape*oncologist	1 17	212.250000 B	171.9815260	1.23	0.2184
shape*oncologist	1 18	177.750000 B	171.9815260	1.03	0.3024
shape*oncologist	1 19	128.750000 B	171.9815260	0.75	0.4548
shape*oncologist	1 20	22.250000 B	171.9815260	0.13	0.8972
shape*oncologist	1 21	-86.250000 B	171.9815260	-0.50	0.6165
shape*oncologist	1 22	-63.750000 B	171.9815260	-0.37	0.7112
shape*oncologist	1 23	38.250000 B	171.9815260	0.22	0.8242
shape*oncologist	1 24	227.250000 B	171.9815260	1.32	0.1877
shape*oncologist	1 25	4.500000 B	171.9815260	0.03	0.9791
shape*oncologist	1 26	0.000000 B	.	.	.
shape*oncologist	2 1	215.750000 B	171.9815260	1.25	0.2109
shape*oncologist	2 2	150.000000 B	171.9815260	0.87	0.3840
shape*oncologist	2 3	237.750000 B	171.9815260	1.38	0.1682
shape*oncologist	2 4	-11.500000 B	171.9815260	-0.07	0.9467
shape*oncologist	2 5	225.500000 B	171.9815260	1.31	0.1911
shape*oncologist	2 6	-302.750000 B	171.9815260	-1.76	0.0797
shape*oncologist	2 7	118.250000 B	171.9815260	0.69	0.4924
shape*oncologist	2 8	117.500000 B	171.9815260	0.68	0.4951
shape*oncologist	2 9	96.500000 B	171.9815260	0.56	0.5753
shape*oncologist	2 10	-68.750000 B	171.9815260	-0.40	0.6897
shape*oncologist	2 11	274.250000 B	171.9815260	1.59	0.1121
shape*oncologist	2 12	-100.750000 B	171.9815260	-0.59	0.5586
shape*oncologist	2 13	196.500000 B	171.9815260	1.14	0.2544
shape*oncologist	2 14	148.000000 B	171.9815260	0.86	0.3904
shape*oncologist	2 15	114.250000 B	171.9815260	0.66	0.5071
shape*oncologist	2 16	116.500000 B	171.9815260	0.68	0.4988
shape*oncologist	2 17	175.000000 B	171.9815260	1.02	0.3099
shape*oncologist	2 18	116.500000 B	171.9815260	0.68	0.4988
shape*oncologist	2 19	45.500000 B	171.9815260	0.26	0.7916
shape*oncologist	2 20	96.000000 B	171.9815260	0.56	0.5772

shape*oncologist 2 21	-21.250000 B	171.9815260	-0.12	0.9018
shape*oncologist 2 22	10.250000 B	171.9815260	0.06	0.9525
shape*oncologist 2 23	-48.750000 B	171.9815260	-0.28	0.7771
shape*oncologist 2 24	135.000000 B	171.9815260	0.78	0.4333
shape*oncologist 2 25	111.500000 B	171.9815260	0.65	0.5174
shape*oncologist 2 26	0.000000 B	.	.	.
shape*oncologist 3 1	0.000000 B	.	.	.
shape*oncologist 3 2	0.000000 B	.	.	.
shape*oncologist 3 3	0.000000 B	.	.	.
shape*oncologist 3 4	0.000000 B	.	.	.
shape*oncologist 3 5	0.000000 B	.	.	.
shape*oncologist 3 6	0.000000 B	.	.	.
shape*oncologist 3 7	0.000000 B	.	.	.
shape*oncologist 3 8	0.000000 B	.	.	.
shape*oncologist 3 9	0.000000 B	.	.	.
shape*oncologist 3 10	0.000000 B	.	.	.
shape*oncologist 3 11	0.000000 B	.	.	.
shape*oncologist 3 12	0.000000 B	.	.	.
shape*oncologist 3 13	0.000000 B	.	.	.
shape*oncologist 3 14	0.000000 B	.	.	.
shape*oncologist 3 15	0.000000 B	.	.	.
shape*oncologist 3 16	0.000000 B	.	.	.
shape*oncologist 3 17	0.000000 B	.	.	.
shape*oncologist 3 18	0.000000 B	.	.	.
shape*oncologist 3 19	0.000000 B	.	.	.
shape*oncologist 3 20	0.000000 B	.	.	.
shape*oncologist 3 21	0.000000 B	.	.	.
shape*oncologist 3 22	0.000000 B	.	.	.
shape*oncologist 3 23	0.000000 B	.	.	.
shape*oncologist 3 24	0.000000 B	.	.	.
shape*oncologist 3 25	0.000000 B	.	.	.
shape*oncologist 3 26	0.000000 B	.	.	.

NOTE: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter 'B' are not uniquely estimable.

=====
The SAS System

3

The GLM Procedure

Source	Type III Expected Mean Square
shape	Var(Error) + 4 Var(shape*oncologist) + Q(shape)
oncologist	Var(Error) + 4 Var(shape*oncologist) + 12 Var(oncologist)
shape*oncologist	Var(Error) + 4 Var(shape*oncologist)

=====
The SAS System

4

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: size

Source	DF	Type III SS	Mean Square	F Value	Pr > F
shape	2	12273864	6136932	211.58	<.0001
oncologist	25	13851803	554072	19.10	<.0001
Error	50	1450264	29005		
Error: MS(shape*oncologist)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
shape*oncologist	50	1450264	29005	0.98	0.5162
Error: MS(Error)	234	6921169	29578		

(6.) Comparisons to a two-way fixed effects ANOVA:

How do the PROC GLM results shown below, with both shape and oncologist taken to be fixed factors, compare to the results when oncologist was treated as random? Have the sums of squares or mean squares changed? How have the expected mean squares changed? Have the estimates of each component of variance changed?

```
%INCLUDE "onc.readdata.sas";

PROC GLM DATA=sorted;
  CLASS shape oncologist;
  MODEL size = shape oncologist shape*oncologist / SOLUTION;
RUN;
```

=====

The SAS System 1

The GLM Procedure

Class Level Information

Class	Levels	Values
shape	3	1 2 3
oncologist	26	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

Number of Observations Read 312
 Number of Observations Used 312

=====

The SAS System 2

The GLM Procedure

Dependent Variable: size

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	77	27575930.49	358128.97	12.11	<.0001
Error	234	6921169.00	29577.65		
Corrected Total	311	34497099.49			

R-Square	Coeff Var	Root MSE	size Mean
0.799370	13.92852	171.9815	1234.744

Source	DF	Type I SS	Mean Square	F Value	Pr > F
shape	2	12273863.58	6136931.79	207.49	<.0001
oncologist	25	13851803.32	554072.13	18.73	<.0001
shape*oncologist	50	1450263.58	29005.27	0.98	0.5162

Source	DF	Type III SS	Mean Square	F Value	Pr > F
shape	2	12273863.58	6136931.79	207.49	<.0001
oncologist	25	13851803.32	554072.13	18.73	<.0001
shape*oncologist	50	1450263.58	29005.27	0.98	0.5162

Standard

Parameter		Estimate	Error	t Value	Pr > t
Intercept		1391.250000 B	85.9907630	16.18	<.0001
shape	1	-493.500000 B	121.6093033	-4.06	<.0001
shape	2	-350.000000 B	121.6093033	-2.88	0.0044
shape	3	0.000000 B	.	.	.
oncologist	1	-293.750000 B	121.6093033	-2.42	0.0165
oncologist	2	-72.500000 B	121.6093033	-0.60	0.5516
oncologist	3	-215.500000 B	121.6093033	-1.77	0.0777
oncologist	4	88.750000 B	121.6093033	0.73	0.4662
oncologist	5	383.750000 B	121.6093033	3.16	0.0018
oncologist	6	895.250000 B	121.6093033	7.36	<.0001
oncologist	7	121.750000 B	121.6093033	1.00	0.3178
oncologist	8	102.750000 B	121.6093033	0.84	0.3990
oncologist	9	-17.750000 B	121.6093033	-0.15	0.8841
oncologist	10	590.000000 B	121.6093033	4.85	<.0001
oncologist	11	88.000000 B	121.6093033	0.72	0.4700
oncologist	12	199.500000 B	121.6093033	1.64	0.1022
oncologist	13	-94.750000 B	121.6093033	-0.78	0.4367
oncologist	14	64.000000 B	121.6093033	0.53	0.5992
oncologist	15	84.250000 B	121.6093033	0.69	0.4891
oncologist	16	-102.750000 B	121.6093033	-0.84	0.3990
oncologist	17	158.750000 B	121.6093033	1.31	0.1930
oncologist	18	18.250000 B	121.6093033	0.15	0.8808
oncologist	19	-267.000000 B	121.6093033	-2.20	0.0291
oncologist	20	-20.000000 B	121.6093033	-0.16	0.8695
oncologist	21	255.000000 B	121.6093033	2.10	0.0371
oncologist	22	346.000000 B	121.6093033	2.85	0.0048
oncologist	23	290.000000 B	121.6093033	2.38	0.0179
oncologist	24	-282.750000 B	121.6093033	-2.33	0.0209
oncologist	25	132.500000 B	121.6093033	1.09	0.2770
oncologist	26	0.000000 B	.	.	.
shape*oncologist	1 1	37.750000 B	171.9815260	0.22	0.8265
shape*oncologist	1 2	-62.750000 B	171.9815260	-0.36	0.7155
shape*oncologist	1 3	63.750000 B	171.9815260	0.37	0.7112
shape*oncologist	1 4	6.000000 B	171.9815260	0.03	0.9722
shape*oncologist	1 5	22.250000 B	171.9815260	0.13	0.8972
shape*oncologist	1 6	-321.750000 B	171.9815260	-1.87	0.0626
shape*oncologist	1 7	-3.500000 B	171.9815260	-0.02	0.9838
shape*oncologist	1 8	64.750000 B	171.9815260	0.38	0.7069
shape*oncologist	1 9	63.750000 B	171.9815260	0.37	0.7112
shape*oncologist	1 10	-280.250000 B	171.9815260	-1.63	0.1045
shape*oncologist	1 11	-27.250000 B	171.9815260	-0.16	0.8742
shape*oncologist	1 12	-132.250000 B	171.9815260	-0.77	0.4427
shape*oncologist	1 13	-65.250000 B	171.9815260	-0.38	0.7047
shape*oncologist	1 14	57.500000 B	171.9815260	0.33	0.7384
shape*oncologist	1 15	98.250000 B	171.9815260	0.57	0.5684
shape*oncologist	1 16	39.500000 B	171.9815260	0.23	0.8185
shape*oncologist	1 17	212.250000 B	171.9815260	1.23	0.2184
shape*oncologist	1 18	177.750000 B	171.9815260	1.03	0.3024
shape*oncologist	1 19	128.750000 B	171.9815260	0.75	0.4548
shape*oncologist	1 20	22.250000 B	171.9815260	0.13	0.8972
shape*oncologist	1 21	-86.250000 B	171.9815260	-0.50	0.6165
shape*oncologist	1 22	-63.750000 B	171.9815260	-0.37	0.7112
shape*oncologist	1 23	38.250000 B	171.9815260	0.22	0.8242
shape*oncologist	1 24	227.250000 B	171.9815260	1.32	0.1877
shape*oncologist	1 25	4.500000 B	171.9815260	0.03	0.9791
shape*oncologist	1 26	0.000000 B	.	.	.
shape*oncologist	2 1	215.750000 B	171.9815260	1.25	0.2109
shape*oncologist	2 2	150.000000 B	171.9815260	0.87	0.3840
shape*oncologist	2 3	237.750000 B	171.9815260	1.38	0.1682
shape*oncologist	2 4	-11.500000 B	171.9815260	-0.07	0.9467
shape*oncologist	2 5	225.500000 B	171.9815260	1.31	0.1911
shape*oncologist	2 6	-302.750000 B	171.9815260	-1.76	0.0797
shape*oncologist	2 7	118.250000 B	171.9815260	0.69	0.4924
shape*oncologist	2 8	117.500000 B	171.9815260	0.68	0.4951
shape*oncologist	2 9	96.500000 B	171.9815260	0.56	0.5753
shape*oncologist	2 10	-68.750000 B	171.9815260	-0.40	0.6897
shape*oncologist	2 11	274.250000 B	171.9815260	1.59	0.1121
shape*oncologist	2 12	-100.750000 B	171.9815260	-0.59	0.5586
shape*oncologist	2 13	196.500000 B	171.9815260	1.14	0.2544
shape*oncologist	2 14	148.000000 B	171.9815260	0.86	0.3904
shape*oncologist	2 15	114.250000 B	171.9815260	0.66	0.5071
shape*oncologist	2 16	116.500000 B	171.9815260	0.68	0.4988
shape*oncologist	2 17	175.000000 B	171.9815260	1.02	0.3099
shape*oncologist	2 18	116.500000 B	171.9815260	0.68	0.4988
shape*oncologist	2 19	45.500000 B	171.9815260	0.26	0.7916

shape*oncologist 2 20	96.000000 B	171.9815260	0.56	0.5772
shape*oncologist 2 21	-21.250000 B	171.9815260	-0.12	0.9018
shape*oncologist 2 22	10.250000 B	171.9815260	0.06	0.9525
shape*oncologist 2 23	-48.750000 B	171.9815260	-0.28	0.7771
shape*oncologist 2 24	135.000000 B	171.9815260	0.78	0.4333
shape*oncologist 2 25	111.500000 B	171.9815260	0.65	0.5174
shape*oncologist 2 26	0.000000 B	.	.	.
shape*oncologist 3 1	0.000000 B	.	.	.
shape*oncologist 3 2	0.000000 B	.	.	.
shape*oncologist 3 3	0.000000 B	.	.	.
shape*oncologist 3 4	0.000000 B	.	.	.
shape*oncologist 3 5	0.000000 B	.	.	.
shape*oncologist 3 6	0.000000 B	.	.	.
shape*oncologist 3 7	0.000000 B	.	.	.
shape*oncologist 3 8	0.000000 B	.	.	.
shape*oncologist 3 9	0.000000 B	.	.	.
shape*oncologist 3 10	0.000000 B	.	.	.
shape*oncologist 3 11	0.000000 B	.	.	.
shape*oncologist 3 12	0.000000 B	.	.	.
shape*oncologist 3 13	0.000000 B	.	.	.
shape*oncologist 3 14	0.000000 B	.	.	.
shape*oncologist 3 15	0.000000 B	.	.	.
shape*oncologist 3 16	0.000000 B	.	.	.
shape*oncologist 3 17	0.000000 B	.	.	.
shape*oncologist 3 18	0.000000 B	.	.	.
shape*oncologist 3 19	0.000000 B	.	.	.
shape*oncologist 3 20	0.000000 B	.	.	.
shape*oncologist 3 21	0.000000 B	.	.	.
shape*oncologist 3 22	0.000000 B	.	.	.
shape*oncologist 3 23	0.000000 B	.	.	.
shape*oncologist 3 24	0.000000 B	.	.	.
shape*oncologist 3 25	0.000000 B	.	.	.
shape*oncologist 3 26	0.000000 B	.	.	.

NOTE: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter 'B' are not uniquely estimable.