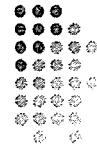


Dunnett's one side test

- When the one side 95% confidence intervals (CI) for the effect are constructed, the lower limit being over 0 corresponds to the statistically significance with $\alpha = 5\%$.
- There are several ways to construct the CI.
- In this presentation, I used the CI based on the Dunnett's one side test for the values of estimates.

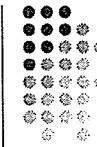
48



Dunnett's one side test

- Dunnett's test assumes the followings:
 - Estimates are independent;
 - Estimates are normally distributed;
 - Estimates have constant variance.

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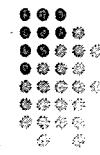


Dunnett's one side test

| Estimate | Parameter | Region | Lab. | Comparison | | | | |
|-----------|------------|---------|------|------------|-------|-------|-------|------|
| | | | | L - V | H - V | Lower | Diff. | Sia. |
| Mean(Obs) | % tail DNA | Liver | 1 | 10.5 | 18.5 | 22.5 | 30.5 | Sia. |
| | | | 2 | 8.1 | 14.5 | 32.1 | 38.5 | Sia. |
| | | | 3 | 17.5 | 22.5 | 43.5 | 48.5 | Sia. |
| | | | 4 | 38.6 | 45.5 | 45.1 | 52 | Sia. |
| | | | 5 | 37.5 | 45.5 | 54.6 | 62 | Sia. |
| | Stomach | Stomach | 1 | 8.1 | 16.5 | 13 | 21 | Sia. |
| | | | 2 | 3.2 | 10.5 | 13.4 | 20 | Sia. |
| | | | 3 | 27.8 | 30.5 | 42.2 | 45.5 | Sia. |
| | | | 4 | 32.7 | 39.5 | 42.4 | 49 | Sia. |
| | | | 5 | 45.6 | 55.5 | 52.4 | 62 | Sia. |

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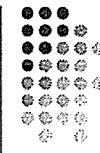
Discussion for statistical test



- We can use the tests that have more powerful tests. However, to construct the CI is sometimes difficult.
- We could relax the above assumption by using other approaches, such as the mixed effect model and the simulation based CI. We need further examinations.

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Discussion for statistical test



- We could do statistical tests directory for the values of a parameter to obtain effects, using the GEE or the mixed effect model. We need further examinations for these methods.

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One side Dunnett's test

Comparison

| Estimate | Parameter | Region | L - V | | | H - V | | |
|-----------------------|-----------|--------|-------|-------|---------|-------|-------|---------|
| | | | Lab | Lower | Dif. f. | Sig. | Lower | Dif. f. |
| Mean (Obs % tail DNA) | Liver | 1 | 10.5 | 18.4 | Sig | 22.5 | 30.3 | Sig |
| | | 2 | 8.1 | 14.9 | Sig | 32.1 | 38.8 | Sig |
| | | 3 | 17.5 | 22.3 | Sig | 43.5 | 48.3 | Sig |
| | | 4 | 38.6 | 45.5 | Sig | 45.1 | 52.0 | Sig |
| | | 5 | 37.5 | 45.0 | Sig | 54.6 | 62.1 | Sig |
| Stomach | Stomach | 1 | 8.1 | 16.6 | Sig | 13.0 | 21.5 | Sig |
| | | 2 | 3.2 | 10.6 | Sig | 13.4 | 20.8 | Sig |
| | | 3 | 27.8 | 30.9 | Sig | 42.2 | 45.3 | Sig |
| | | 4 | 32.7 | 39.7 | Sig | 42.4 | 49.4 | Sig |
| | | 5 | 45.6 | 55.3 | Sig | 52.4 | 62.0 | Sig |
| Olive tail moment | Liver | 1 | 1.6 | 4.8 | Sig | 6.6 | 9.8 | Sig |

Comparison

| Estimate | Parameter | Region | Lab | L - V | | | H - V | | |
|----------|-------------|--------|------|-------|------|------|-------|------|------|
| | | | | Lower | Dif. | Sig. | Lower | Dif. | Sig. |
| | | | 2 | 3.3 | 8.2 | Sig | 17.0 | 21.9 | Sig |
| | | | 3 | -0.2 | 5.1 | NS | 19.0 | 24.3 | Sig |
| | | | 4 | 10.0 | 13.1 | Sig | 14.0 | 17.2 | Sig |
| | | | 5 | 7.4 | 11.6 | Sig | 16.3 | 20.4 | Sig |
| | Stomach | 1 | 1.6 | 4.2 | Sig | 3.2 | 5.8 | Sig | |
| | | 2 | 0.5 | 3.3 | Sig | 4.2 | 7.0 | Sig | |
| | | 3 | 7.3 | 10.6 | Sig | 17.2 | 20.5 | Sig | |
| | | 4 | 9.4 | 12.2 | Sig | 14.2 | 16.9 | Sig | |
| | | 5 | 14.3 | 22.2 | Sig | 16.6 | 24.5 | Sig | |
| | Tail length | Liver | 1 | 13.2 | 23.5 | Sig | 24.8 | 35.1 | Sig |
| | | 2 | 73.8 | 113. | Sig | 106. | 146. | Sig | |
| | | 3 | 34.3 | 49.6 | Sig | 104. | 120. | Sig | |
| | | | | | | | 8 | 1 | |

Comparison

| | | | L - V | H - V | | | | | |
|-----------------|---------------|---------|------------|-------|------|-------------|------|------|-----|
| Estimate | Parameter | Region | Lab vs Low | Dif. | Sig. | Lab vs High | Dif. | Sig. | |
| Median(0 bs) | % tail DNA | Liver | 1 | 26.7 | 35.7 | Sig | 32.1 | 41.2 | Sig |
| | | Stomach | 2 | 44.5 | 57.1 | Sig | 53.0 | 65.6 | Sig |
| | | Stomach | 3 | 7.2 | 13.9 | Sig | 9.9 | 16.6 | Sig |
| | | Stomach | 4 | -2.3 | 5.9 | NS | 9.4 | 17.7 | Sig |
| | | Stomach | 5 | 43.7 | 54.9 | Sig | 70.7 | 81.9 | Sig |
| | | Liver | 1 | 21.4 | 26.2 | Sig | 24.7 | 29.5 | Sig |
| | | Liver | 2 | 41.4 | 62.6 | Sig | 25.9 | 47.2 | Sig |
| | | Liver | 3 | 11.8 | 21.0 | Sig | 23.8 | 33.1 | Sig |
| | | Liver | 4 | 6.7 | 15.4 | Sig | 34.3 | 43.0 | Sig |
| | | Liver | 5 | 16.8 | 23.0 | Sig | 43.6 | 49.8 | Sig |
| | | Bladder | 1 | 46.0 | 51.8 | Sig | 53.8 | 59.5 | Sig |
| | | Bladder | 2 | 38.0 | 46.0 | Sig | 55.5 | 63.6 | Sig |

Comparison

| | | | L - V | | | H - V | | |
|----------------------|-----------|-----|--------|---------|------|--------|---------|------|
| Estimating Parameter | Regime | Lab | Low f. | Dif. f. | Sig. | Low f. | Dif. f. | Sig. |
| Stomach | Stoma ch. | 1 | 9.5 | 19.7 | Sig | 16.3 | 26.6 | Sig |
| Stomach | Stoma ch. | 2 | -1.3 | 7.7 | NS | 12.4 | 21.3 | Sig |
| Olive tail | Liver | 3 | 27.3 | 31.4 | Sig | 41.2 | 45.3 | Sig |
| Olive tail | Liver | 4 | 41.6 | 48.5 | Sig | 52.2 | 59.1 | Sig |
| Olive tail | Liver | 5 | 48.2 | 58.2 | Sig | 54.8 | 64.7 | Sig |
| Olive tail moment | Liver | 1 | 1.3 | 4.5 | Sig | 6.2 | 9.4 | Sig |
| Olive tail moment | Liver | 2 | 2.2 | 7.9 | Sig | 17.0 | 22.7 | Sig |
| Olive tail moment | Liver | 3 | -2.9 | 4.8 | NS | 14.3 | 21.9 | Sig |
| Olive tail moment | Liver | 4 | 11.3 | 14.3 | Sig | 16.3 | 19.3 | Sig |
| Olive tail moment | Liver | 5 | 6.8 | 11.2 | Sig | 16.2 | 20.5 | Sig |
| Stomach | Stoma ch. | 1 | 1.8 | 4.6 | Sig | 3.9 | 6.7 | Sig |
| Stomach | Stoma ch. | 2 | -0.7 | 2.3 | NS | 3.7 | 6.7 | Sig |

Comparison

| Estimate | Parameter | Region | Lab | | Dif. | Sig. | Low | | Dif. | Sig. |
|----------|-------------|--------|-------|-------|-------|------|-------|-------|------|------|
| | | | Lower | Upper | | | Lower | Upper | | |
| Weight | Body weight | V | 3 | 4.8 | 8.3 | Sig | 14.0 | 17.4 | Sig | |
| Weight | Body weight | H | 4 | 11.3 | 14.2 | Sig | 16.4 | 19.4 | Sig | |
| Weight | Brain | V | 5 | 13.5 | 21.5 | Sig | 15.7 | 23.8 | Sig | |
| Weight | Brain | H | 10 | 13.0 | 22.9 | Sig | 24.7 | 34.7 | Sig | |
| Weight | Tail length | V | 2 | 78.3 | 133.6 | Sig | 109.6 | 164.9 | Sig | |
| Weight | Tail length | H | 3 | 26.6 | 49.8 | Sig | 98.9 | 122.1 | Sig | |
| Weight | Heart | V | 4 | 28.0 | 37.1 | Sig | 34.0 | 43.0 | Sig | |
| Weight | Heart | H | 5 | 48.6 | 61.1 | Sig | 57.9 | 70.5 | Sig | |
| Weight | Stomach | V | 1 | 8.9 | 16.6 | Sig | 12.2 | 20.0 | Sig | |
| Weight | Stomach | H | 2 | -3.0 | 5.5 | NS | 7.8 | 16.3 | Sig | |
| Weight | Liver | V | 3 | 45.6 | 58.2 | Sig | 69.1 | 81.7 | Sig | |
| Weight | Liver | H | 4 | 20.8 | 26.4 | Sig | 23.4 | 28.9 | Sig | |

| Estimate | Parameter | Region | Lab | | Dif. | Sig. | Comparison | |
|-------------------|-----------|--------|------|------|------|------|------------|-----|
| | | | Mean | SD | | | Mean | SD |
| Mean (Log % tail) | Liver DNA | V | 40.3 | 62.0 | Sig | 24.7 | 46.4 | Sig |
| Mean (Log % tail) | Liver DNA | H | 1.8 | 2.1 | Sig | 2.2 | 2.6 | Sig |
| Mean (Log % tail) | Stomach | V | 1.2 | 1.9 | Sig | 2.8 | 3.4 | Sig |
| Mean (Log % tail) | Stomach | H | 0.3 | 0.41 | Sig | 5.0 | 5.6 | Sig |
| Mean (Log % tail) | Stomach | V | 0.4 | 0.41 | Sig | 4.2 | 5.7 | Sig |
| Mean (Log % tail) | Stomach | H | 0.5 | 0.5 | Sig | 5.4 | 5.7 | Sig |
| Mean (Log % tail) | Stomach | V | 0.8 | 1.2 | Sig | 0.9 | 1.3 | Sig |
| Mean (Log % tail) | Stomach | H | 0.8 | 1.2 | Sig | 1.4 | 1.9 | Sig |
| Mean (Log % tail) | Stomach | V | 2.6 | 3.0 | Sig | 3.1 | 3.4 | Sig |
| Mean (Log % tail) | Stomach | H | 2.1 | 2.8 | Sig | 2.3 | 2.9 | Sig |
| Mean (Log % tail) | Stomach | V | 2.8 | 3.3 | Sig | 2.9 | 3.4 | Sig |
| Olive tail moment | Liver | V | 2.1 | 2.6 | Sig | 2.8 | 3.3 | Sig |

Comparison

| Estimate | Parameter | Region | Lab | Lower f. | Upper f. | L - V | | H - V | |
|----------|-------------|--------|-----|----------|----------|-------|------|-------|------|
| | | | | | | Dif. | Sig. | Dif. | Sig. |
| Mean | Weight | 2 | 2.3 | 3.1 | Sig | 3.3 | 4.0 | Sig | |
| Mean | Length | 3 | 4.3 | 4.9 | Sig | 5.8 | 6.4 | Sig | |
| Mean | Width | 4 | 4.2 | 5.6 | Sig | 4.5 | 5.8 | Sig | |
| Mean | Height | 5 | 5.3 | 5.6 | Sig | 5.8 | 6.2 | Sig | |
| Mean | Stomach | 1 | 1.0 | 1.6 | Sig | 1.2 | 1.7 | Sig | |
| Mean | Bladder | 2 | 0.7 | 1.2 | Sig | 1.4 | 1.9 | Sig | |
| Mean | Uterus | 3 | 3.1 | 3.5 | Sig | 3.8 | 4.2 | Sig | |
| Mean | Heart | 4 | 2.4 | 3.0 | Sig | 2.7 | 3.3 | Sig | |
| Mean | Liver | 5 | 3.2 | 3.7 | Sig | 3.3 | 3.9 | Sig | |
| Mean | Tail length | 1 | 1.1 | 1.5 | Sig | 1.4 | 1.8 | Sig | |
| Mean | Testes | 2 | 1.6 | 2.3 | Sig | 1.8 | 2.5 | Sig | |
| Mean | Bladder | 3 | 0.8 | 1.0 | Sig | 1.4 | 1.6 | Sig | |

Comparison

| | | | L - V | H - V |
|-------------|------------|-----------------|--------|---------|
| Estimate | Parameter | Region | Low f. | Dif. f. |
| | | Liver | 0.5 | 0.7 |
| | | Stomach | 1.4 | 1.7 |
| | | Small Intestine | 1.5 | 2.1 |
| | | Large Intestine | 1.0 | 1.3 |
| | | Stomach | 1.1 | 1.4 |
| | | Small Intestine | 0.0 | 0.2 |
| | | Large Intestine | 0.2 | 0.4 |
| | | Stomach | 0.8 | 0.9 |
| | | Small Intestine | 0.3 | 0.4 |
| | | Large Intestine | 0.4 | 0.5 |
| | | Stomach | 0.5 | 0.7 |
| Median(Log) | % tail DNA | Liver | 1.4 | 1.8 |
| | | Stomach | 1.1 | 1.5 |
| | | Small Intestine | 2.2 | 2.0 |
| | | Large Intestine | 2.5 | 2.4 |
| | | Stomach | 2.1 | 2.9 |
| | | Small Intestine | 3.2 | 3.6 |
| | | Large Intestine | 3.5 | 4.6 |
| | | Stomach | 3.3 | 4.1 |
| | | Small Intestine | 3.6 | 5.7 |
| | | Large Intestine | 4.0 | 5.4 |
| | | Stomach | 3.5 | 5.0 |
| | | Small Intestine | 4.5 | 5.4 |
| | | Large Intestine | 5.0 | 5.7 |

Comparison

L - V H - V

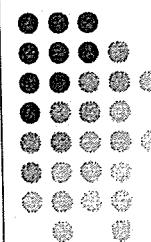
| Estimate | Parameter | Region | Lab | Low | Dif. | Sig. | Low | Dif. | Sig. |
|----------|-------------------|--------|------|-----|------|------|-----|------|------|
| | Stomach | 1 | -0.5 | 0.9 | Sig | 0.7 | 1.0 | Sig | |
| | | 2 | 0.7 | 1.1 | Sig | 1.4 | 1.8 | Sig | |
| | | 3 | 2.2 | 2.5 | Sig | 2.5 | 2.8 | Sig | |
| | | 4 | 1.9 | 2.5 | Sig | 2.0 | 2.7 | Sig | |
| | | 5 | 2.7 | 3.2 | Sig | 2.8 | 3.3 | Sig | |
| | Olive tail moment | Liver | 1 | 1.8 | 2.2 | Sig | 2.4 | 2.9 | Sig |
| | | 2 | 2.0 | 2.8 | Sig | 3.0 | 3.8 | Sig | |
| | | 3 | 3.7 | 4.7 | Sig | 5.2 | 6.1 | Sig | |
| | | 4 | 4.5 | 6.0 | Sig | 4.8 | 6.3 | Sig | |
| | | 5 | 5.3 | 5.7 | Sig | 5.9 | 6.3 | Sig | |
| | Stomach | 1 | 0.8 | 1.3 | Sig | 1.1 | 1.6 | Sig | |
| | | 2 | 0.6 | 1.1 | Sig | 1.4 | 1.9 | Sig | |

Comparison

| | | L - V | | | H - V | | | | |
|---------|---------|-------|-----|-----|-------|-----|-----|-----|-----|
| Estimat | Paramet | Regi | Lab | Low | Dif | Sig | Low | Dif | Sig |
| | | | 5 | 0.5 | 0.8 | Sig | 0.4 | 0.7 | Sig |

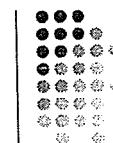
Slide-to-slide variation

Jan 30, 2007
Takashi Omori

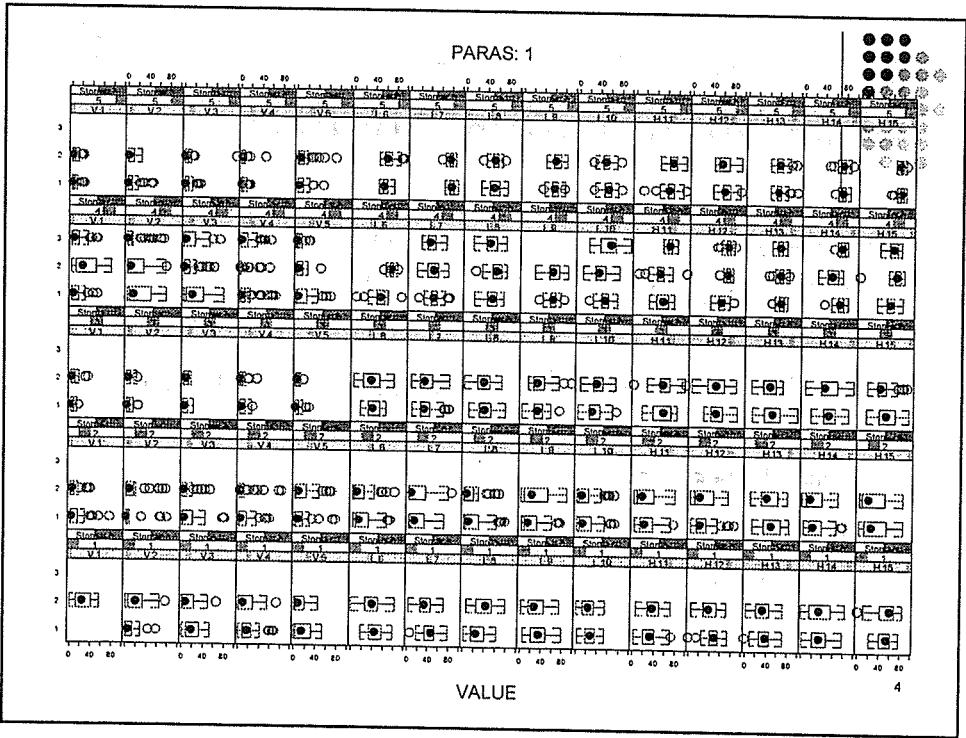
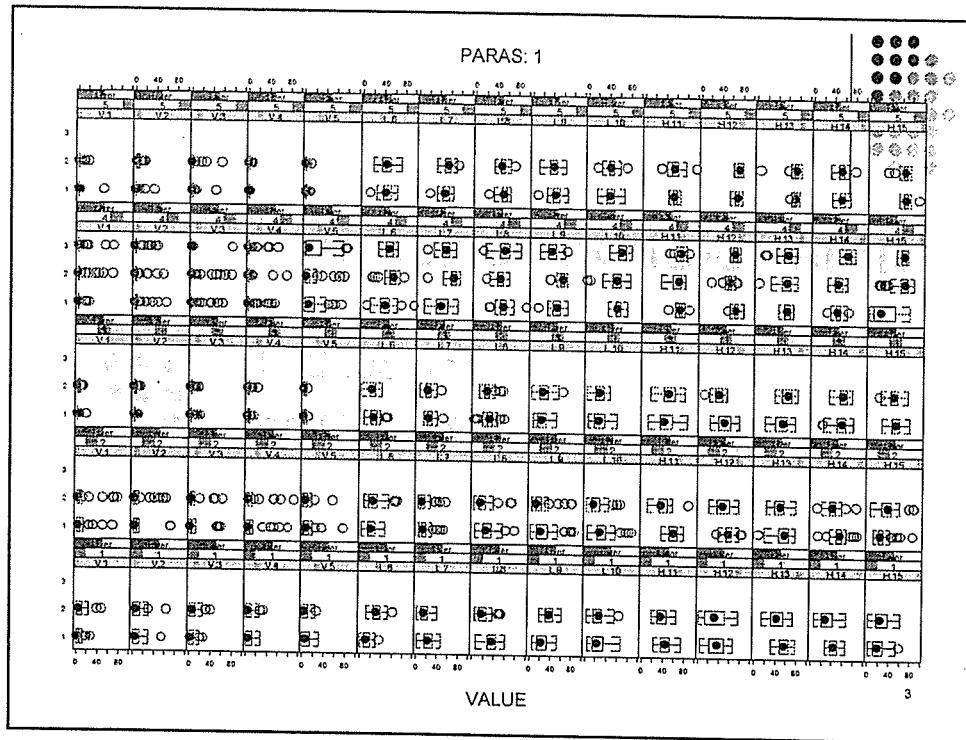


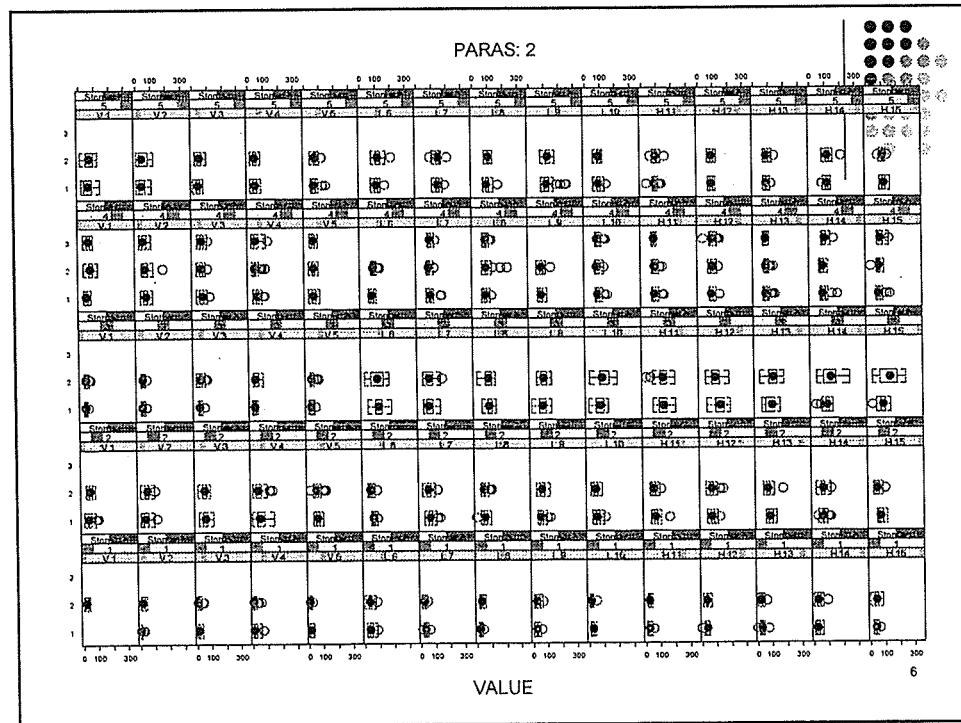
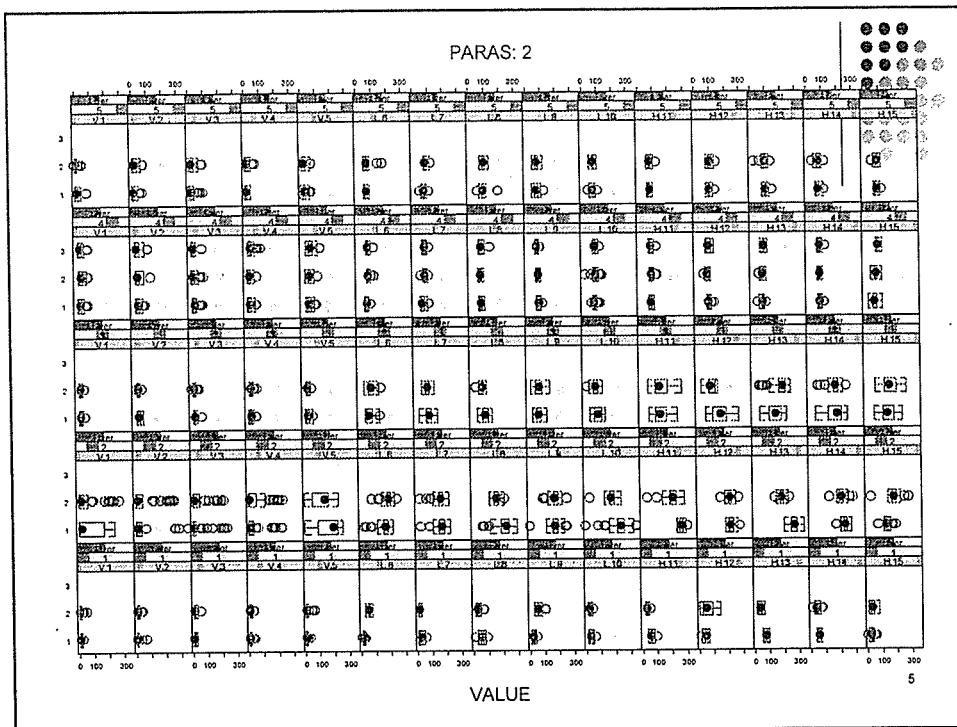
Boxplot of observed values by slide on individual animals

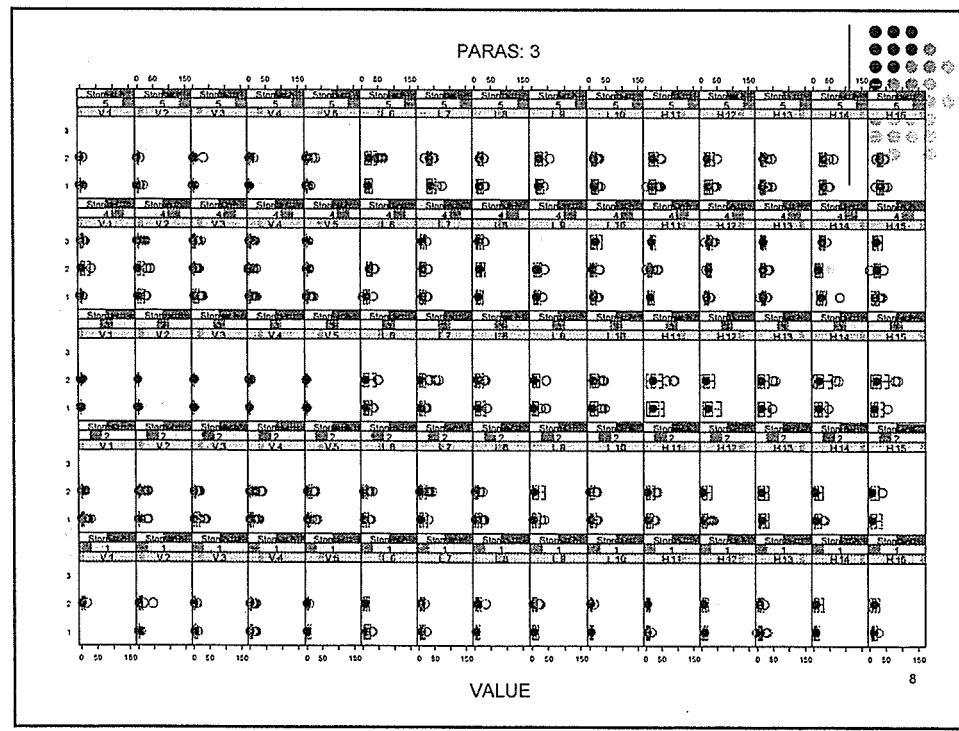
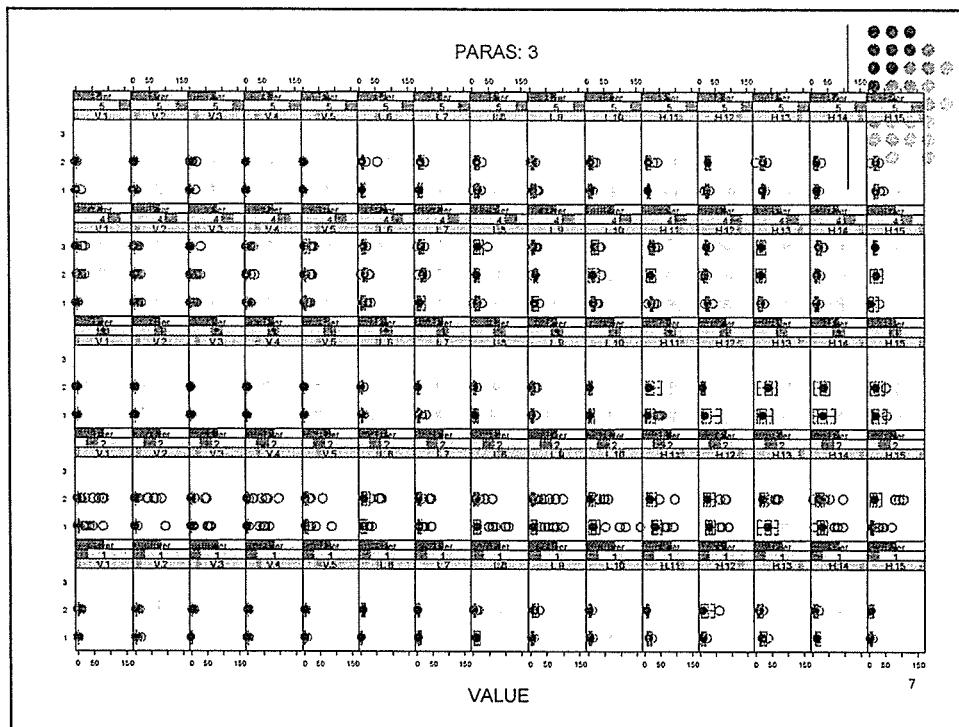
- PARAS
 - 1: % DNA in tail
 - 2: tail length
 - 3: Olive tail moment
- Level 1: Region
 - Liver
 - Stomach
- Level 2: Facility code
 - 1-5
- Level 3: Animal
 - 1-15



2





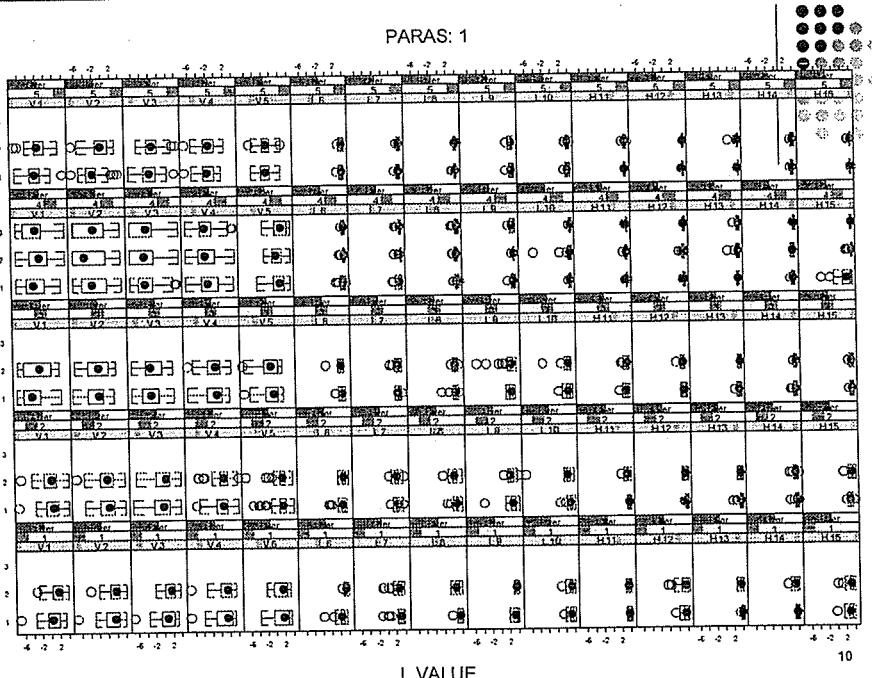


Boxplot of log transformed values by slide on individual animals

- PARAS
 - 1: % DNA in tail
 - 2: tail length
 - 3: Olive tail moment
- Level 1: Region
 - Liver
 - Stomach
- Level 2: Facility code
 - 1-5
- Level 3: Animal
 - 1-15

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PARAS: 1



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