Supplementary Material

Histopathological assessment of Atlantic salmon exposed to calcium oxide particles. A controlled clinical study

Elia Ciani1\*, Kai-Inge Lie2, Marit Stormoen1, Stein Ivar Antonsen3, Even Hjalmar Jørgensen4

1 Department of Production Animal clinical Sciences, Norwegian University of Life Sciences; Ås, Norway

2 Pharmaq Analytiq AS, Bergen, Norway

3 Seacalx AS; Gratangen, Norway

4 Department of Arctic and Marine Biology, The Arctic University of Norway, Tromsø, Norway

\*Corresponding author: elia.ciani@nmbu.no

# Supplementary Data

Supplementary Table 1 Correlation matrix between possible predictors. The variable included in this analysis were water temperature, treatment, and time.

|  |  |  |  |
| --- | --- | --- | --- |
|  | temp | treat | time |
| temperature | 1 |   |   |
| treatment | 0.0043 | 1 |   |
| time | -0.0216 | 0.2134 | 1 |

Supplementary Table 2 Margins from the multilevel ordinal regression models.

|  |  |  |
| --- | --- | --- |
| **Effect of treatment on vascular injuries** |  | **Effect of time on inflammation** |
| Score |  | dy/dx | std. Err | z | p | 95%CI |  | Score | Day | Margin | std. Err | z | p | 95%CI |
| 0 |  | -0.63 | 0.12 | -5.39 | 0.000 | -0.85 | -0.40 |  | 0 | 0 | 0.11 | 0.04 | 2.51 | 0.012 | 0.02 | 0.19 |
| 1 |  | 0.58 | 0.12 | 4.93 | 0.000 | 0.35 | 0.81 |  | 0 | 5 | 0.09 | 0.04 | 2.56 | 0.011 | 0.02 | 0.16 |
| 2 |  | 0.05 | 0.05 | 0.99 | 0.323 | -0.05 | 0.15 |  | 0 | 10 | 0.08 | 0.03 | 2.54 | 0.011 | 0.02 | 0.14 |
|  |  |  |  |  |  |  |  |  | 0 | 15 | 0.07 | 0.03 | 2.45 | 0.014 | 0.01 | 0.12 |
|  |  |  |  |  |  |  |  |  | 0 | 20 | 0.06 | 0.02 | 2.30 | 0.021 | 0.01 | 0.10 |
| **Effect of high temperature over time on hyperplasia** |  | 1 | 25 | 0.05 | 0.02 | 2.13 | 0.033 | 0.00 | 0.09 |
| Score | Day | dy/dx | std. Err | z | p | 95%CI |  | 1 | 20 | 0.04 | 0.02 | 1.95 | 0.051 | 0.00 | 0.08 |
| 0 | 0 | -0.23 | 0.09 | -2.44 | 0.015 | -0.41 | -0.04 |  | 0 | 35 | 0.03 | 0.02 | 1.78 | 0.076 | 0.00 | 0.07 |
| 0 | 5 | -0.24 | 0.10 | -2.50 | 0.012 | -0.43 | -0.05 |  | 0 | 40 | 0.03 | 0.02 | 1.62 | 0.106 | -0.01 | 0.06 |
| 0 | 10 | -0.25 | 0.10 | -2.53 | 0.011 | -0.43 | -0.06 |  | 0 | 45 | 0.02 | 0.02 | 1.48 | 0.140 | -0.01 | 0.05 |
| 0 | 15 | -0.25 | 0.10 | -2.54 | 0.011 | -0.44 | -0.06 |  | 0 | 50 | 0.02 | 0.01 | 1.35 | 0.176 | -0.01 | 0.05 |
| 0 | 20 | -0.24 | 0.10 | -2.52 | 0.012 | -0.43 | -0.05 |  | 0 | 55 | 0.02 | 0.01 | 1.24 | 0.213 | -0.01 | 0.04 |
| 0 | 25 | -0.24 | 0.10 | -2.46 | 0.014 | -0.42 | -0.05 |  | 0 | 60 | 0.01 | 0.01 | 1.15 | 0.250 | -0.01 | 0.04 |
| 0 | 30 | -0.22 | 0.10 | -2.37 | 0.018 | -0.41 | -0.04 |  | 0 | 65 | 0.01 | 0.01 | 1.07 | 0.286 | -0.01 | 0.03 |
| 0 | 35 | -0.21 | 0.09 | -2.24 | 0.025 | -0.39 | -0.03 |  | 0 | 70 | 0.01 | 0.01 | 0.99 | 0.320 | -0.01 | 0.03 |
| 0 | 40 | -0.19 | 0.09 | -2.08 | 0.037 | -0.37 | -0.01 |  | 0 | 75 | 0.01 | 0.01 | 0.93 | 0.352 | -0.01 | 0.02 |
| 0 | 45 | -0.17 | 0.09 | -1.91 | 0.056 | -0.35 | 0.00 |  | 0 | 80 | 0.01 | 0.01 | 0.87 | 0.383 | -0.01 | 0.02 |
| 0 | 50 | -0.15 | 0.09 | -1.73 | 0.083 | -0.33 | 0.02 |  | 1 | 0 | 0.87 | 0.04 | 20.79 | 0.000 | 0.79 | 0.95 |
| 0 | 55 | -0.13 | 0.09 | -1.57 | 0.117 | -0.30 | 0.03 |  | 1 | 5 | 0.88 | 0.04 | 23.28 | 0.000 | 0.81 | 0.96 |
| 0 | 60 | -0.12 | 0.08 | -1.41 | 0.157 | -0.28 | 0.04 |  | 1 | 10 | 0.89 | 0.04 | 24.65 | 0.000 | 0.82 | 0.96 |
| 0 | 65 | -0.10 | 0.08 | -1.28 | 0.200 | -0.25 | 0.05 |  | 1 | 15 | 0.90 | 0.04 | 25.05 | 0.000 | 0.83 | 0.97 |
| 0 | 70 | -0.08 | 0.07 | -1.17 | 0.244 | -0.22 | 0.06 |  | 1 | 20 | 0.90 | 0.04 | 24.87 | 0.000 | 0.83 | 0.98 |
| 0 | 75 | -0.07 | 0.07 | -1.07 | 0.286 | -0.20 | 0.06 |  | 1 | 25 | 0.91 | 0.04 | 24.37 | 0.000 | 0.83 | 0.98 |
| 0 | 80 | -0.06 | 0.06 | -0.98 | 0.326 | -0.17 | 0.06 |  | 1 | 30 | 0.90 | 0.04 | 23.60 | 0.000 | 0.83 | 0.98 |
| 1 | 0 | 0.22 | 0.09 | 2.44 | 0.015 | 0.04 | 0.40 |  | 1 | 35 | 0.90 | 0.04 | 22.50 | 0.000 | 0.82 | 0.98 |
| 1 | 5 | 0.23 | 0.09 | 2.50 | 0.012 | 0.05 | 0.41 |  | 1 | 40 | 0.89 | 0.04 | 20.92 | 0.000 | 0.81 | 0.98 |
| 1 | 10 | 0.23 | 0.09 | 2.53 | 0.011 | 0.05 | 0.42 |  | 1 | 45 | 0.88 | 0.05 | 18.82 | 0.000 | 0.79 | 0.97 |
| 1 | 15 | 0.23 | 0.09 | 2.53 | 0.011 | 0.05 | 0.41 |  | 1 | 50 | 0.87 | 0.05 | 16.30 | 0.000 | 0.77 | 0.97 |
| 1 | 20 | 0.23 | 0.09 | 2.51 | 0.012 | 0.05 | 0.41 |  | 1 | 55 | 0.85 | 0.06 | 13.66 | 0.000 | 0.73 | 0.98 |
| 1 | 25 | 0.22 | 0.09 | 2.45 | 0.014 | 0.04 | 0.39 |  | 1 | 60 | 0.84 | 0.07 | 11.18 | 0.000 | 0.69 | 0.98 |
| 1 | 30 | 0.20 | 0.09 | 2.34 | 0.019 | 0.03 | 0.37 |  | 1 | 65 | 0.81 | 0.09 | 9.03 | 0.000 | 0.64 | 0.99 |
| 1 | 35 | 0.18 | 0.08 | 2.17 | 0.030 | 0.02 | 0.34 |  | 1 | 70 | 0.79 | 0.11 | 7.26 | 0.000 | 0.57 | 1.00 |
| 1 | 40 | 0.15 | 0.08 | 1.92 | 0.054 | 0.00 | 0.31 |  | 1 | 75 | 0.76 | 0.13 | 5.85 | 0.000 | 0.50 | 1.01 |
| 1 | 45 | 0.13 | 0.08 | 1.60 | 0.110 | -0.03 | 0.28 |  | 1 | 80 | 0.73 | 0.15 | 4.74 | 0.000 | 0.43 | 1.03 |
| 1 | 50 | 0.10 | 0.08 | 1.21 | 0.225 | -0.06 | 0.26 |  | 2 | 0 | 0.02 | 0.02 | 1.26 | 0.206 | -0.01 | 0.05 |
| 1 | 55 | 0.07 | 0.08 | 0.80 | 0.424 | -0.10 | 0.23 |  | 2 | 5 | 0.02 | 0.02 | 1.36 | 0.173 | -0.01 | 0.06 |
| 1 | 60 | 0.04 | 0.09 | 0.40 | 0.690 | -0.14 | 0.21 |  | 2 | 10 | 0.03 | 0.02 | 1.47 | 0.143 | -0.01 | 0.07 |
| 1 | 65 | 0.00 | 0.10 | 0.04 | 0.971 | -0.19 | 0.19 |  | 2 | 15 | 0.03 | 0.02 | 1.58 | 0.115 | -0.01 | 0.08 |
| 1 | 70 | -0.03 | 0.10 | -0.27 | 0.784 | -0.23 | 0.18 |  | 2 | 20 | 0.04 | 0.02 | 1.69 | 0.091 | -0.01 | 0.09 |
| 1 | 75 | -0.06 | 0.11 | -0.53 | 0.593 | -0.28 | 0.16 |  | 2 | 25 | 0.05 | 0.03 | 1.80 | 0.072 | 0.00 | 0.10 |
| 1 | 80 | -0.09 | 0.12 | -0.76 | 0.449 | -0.33 | 0.15 |  | 2 | 30 | 0.06 | 0.03 | 1.89 | 0.058 | 0.00 | 0.12 |
| 2 | 0 | 0.01 | 0.01 | 0.90 | 0.369 | -0.01 | 0.02 |  | 2 | 35 | 0.07 | 0.03 | 1.97 | 0.049 | 0.00 | 0.13 |
| 2 | 5 | 0.01 | 0.01 | 0.94 | 0.348 | -0.01 | 0.03 |  | 2 | 40 | 0.08 | 0.04 | 2.01 | 0.044 | 0.00 | 0.16 |
| 2 | 10 | 0.01 | 0.01 | 0.98 | 0.328 | -0.01 | 0.03 |  | 2 | 45 | 0.09 | 0.05 | 2.02 | 0.043 | 0.00 | 0.18 |
| 2 | 15 | 0.01 | 0.01 | 1.02 | 0.308 | -0.01 | 0.04 |  | 2 | 50 | 0.11 | 0.06 | 2.00 | 0.045 | 0.00 | 0.22 |
| 2 | 20 | 0.02 | 0.02 | 1.06 | 0.290 | -0.01 | 0.05 |  | 2 | 55 | 0.13 | 0.07 | 1.96 | 0.050 | 0.00 | 0.26 |
| 2 | 25 | 0.02 | 0.02 | 1.10 | 0.272 | -0.02 | 0.06 |  | 2 | 60 | 0.15 | 0.08 | 1.91 | 0.057 | 0.00 | 0.31 |
| 2 | 30 | 0.03 | 0.02 | 1.13 | 0.256 | -0.02 | 0.07 |  | 2 | 65 | 0.18 | 0.10 | 1.84 | 0.065 | -0.01 | 0.36 |
| 2 | 35 | 0.03 | 0.03 | 1.17 | 0.242 | -0.02 | 0.08 |  | 2 | 70 | 0.20 | 0.11 | 1.78 | 0.075 | -0.02 | 0.43 |
| 2 | 40 | 0.04 | 0.03 | 1.20 | 0.230 | -0.02 | 0.10 |  | 2 | 75 | 0.23 | 0.14 | 1.73 | 0.083 | -0.03 | 0.50 |
| 2 | 45 | 0.05 | 0.04 | 1.23 | 0.219 | -0.03 | 0.12 |  | 2 | 80 | 0.27 | 0.16 | 1.69 | 0.091 | -0.04 | 0.58 |
| 2 | 50 | 0.06 | 0.04 | 1.25 | 0.210 | -0.03 | 0.14 |  |  |  |  |  |  |  |  |  |
| 2 | 55 | 0.07 | 0.05 | 1.28 | 0.202 | -0.04 | 0.17 |  |  |  |  |  |  |  |  |  |
| 2 | 60 | 0.08 | 0.06 | 1.30 | 0.193 | -0.04 | 0.20 |  |  |  |  |  |  |  |  |  |
| 2 | 65 | 0.10 | 0.07 | 1.33 | 0.184 | -0.05 | 0.24 |  |  |  |  |  |  |  |  |  |
| 2 | 70 | 0.11 | 0.08 | 1.36 | 0.173 | -0.05 | 0.27 |  |  |  |  |  |  |  |  |  |
| 2 | 75 | 0.13 | 0.09 | 1.40 | 0.160 | -0.05 | 0.31 |  |  |  |  |  |  |  |  |  |
| 2 | 80 | 0.15 | 0.10 | 1.46 | 0.144 | -0.05 | 0.35 |  |  |  |  |  |  |  |  |  |