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| Title        | Stage- and tissue-specific effect of cyclophosphamide during tooth development        |
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| Citation     | European Journal of Orthodontics. 2019, 41(5), p. 519-530                             |
| Version Type | AM                                                                                    |
| URL          | <a href="https://hdl.handle.net/11094/103599">https://hdl.handle.net/11094/103599</a> |
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| Timing     | M1             | M2             | M3         |
|------------|----------------|----------------|------------|
| Day1, Day2 | Late bell      | Early bell     | Bud        |
| Day4       |                |                | Cap        |
| Day6       |                | Late bell      |            |
| Day8       | Root formation |                | Early bell |
| Day10      |                | Root formation | Late bell  |

|        | BrdU + cells per area |      |         |      |         |                |      |         |      |          |            |       |         |       |           | BrdU + cells per surface unit |      |         |      |         |
|--------|-----------------------|------|---------|------|---------|----------------|------|---------|------|----------|------------|-------|---------|-------|-----------|-------------------------------|------|---------|------|---------|
|        | Epithelial area       |      |         |      |         | Dental papilla |      |         |      |          | Tooth germ |       |         |       |           | Dental papilla                |      |         |      |         |
|        | Control               |      | 100-CPA |      |         | Control        |      | 100-CPA |      |          | Control    |       | 100-CPA |       |           | Control                       |      | 100-CPA |      |         |
| Age    | mean                  | SD   | mean    | SD   | p-value | mean           | SD   | mean    | SD   | p-value  | mean       | SD    | mean    | SD    | p-value   | mean                          | SD   | mean    | SD   | p-value |
| Day6.5 | 200.8                 | 41.7 | 219.5   | 73.5 | 0.63223 | 123.7          | 67.2 | 156.5   | 60.9 | 0.43729  | 324.5      | 101.3 | 376.0   | 114.7 | 0.46911   | 60.7                          | 28.9 | 60.0    | 9.0  | 0.91517 |
| Day7   | 217.3                 | 60.1 | 195.2   | 29.1 | 0.47485 | 174.0          | 56.3 | 123.3   | 15.1 | 0.09977  | 391.3      | 113.1 | 318.5   | 31.0  | 0.21409   | 72.8                          | 11.2 | 79.2    | 10.2 | 0.37035 |
| Day8   | 260.7                 | 32.1 | 117.5   | 28.4 | 0.00002 | 228.0          | 25.5 | 23.5    | 10.5 | 0.000001 | 488.7      | 52.7  | 141.0   | 26.4  | 0.0000001 | 39.3                          | 11.9 | 27.3    | 7.3  | 0.08276 |
| Day10  | 108.2                 | 13.5 | 39.3    | 16.6 | 0.00003 | 103.2          | 45.5 | 1.7     | 1.1  | 0.00414  | 211.3      | 48.3  | 41.0    | 16.6  | 0.0003    | 23.5                          | 4.6  | 5.3     | 2.2  | 0.00001 |

|        | Ki67 + cells per area |       |         |      |         |                |      |         |      |         |            |       |         |       |         | Ki67 + cells per surface unit |      |         |      |         |
|--------|-----------------------|-------|---------|------|---------|----------------|------|---------|------|---------|------------|-------|---------|-------|---------|-------------------------------|------|---------|------|---------|
|        | Epithelial area       |       |         |      |         | Dental papilla |      |         |      |         | Tooth germ |       |         |       |         | Dental papilla                |      |         |      |         |
|        | Control               |       | 100-CPA |      |         | Control        |      | 100-CPA |      |         | Control    |       | 100-CPA |       |         | Control                       |      | 100-CPA |      |         |
| Age    | mean                  | SD    | mean    | SD   | p-value | mean           | SD   | mean    | SD   | p-value | mean       | SD    | mean    | SD    | p-value | mean                          | SD   | mean    | SD   | p-value |
| Day6.5 | 376.5                 | 126.2 | 286.0   | 64.1 | 0.18415 | 194.8          | 82.4 | 181.2   | 56.1 | 0.76558 | 571.2      | 202.3 | 467.2   | 115.5 | 0.34168 | 98.7                          | 28.9 | 91.8    | 27.9 | 0.71171 |
| Day7   | 368.8                 | 40.6  | 283.2   | 48.5 | 0.01271 | 283.3          | 32.6 | 155.3   | 19.4 | 0.00002 | 652.2      | 50.1  | 438.5   | 55.7  | 0.00008 | 97.8                          | 6.9  | 78.7    | 8.1  | 0.00242 |
| Day8   | 440.8                 | 52.4  | 254.8   | 21.7 | 0.00016 | 429.7          | 75.8 | 69.0    | 13.7 | 0.00014 | 870.5      | 106.2 | 323.8   | 32.4  | 0.00003 | 80.8                          | 14.1 | 63.7    | 13.3 | 0.07649 |
| Day10  | 265.8                 | 57.2  | 97.7    | 20.2 | 0.00081 | 206.8          | 28.3 | 5.3     | 5.3  | 0.00002 | 472.7      | 84.1  | 103.0   | 22.8  | 0.00008 | 48.2                          | 9.4  | 10.8    | 2.7  | 0.00014 |

|        | TUNEL + cells per area |     |         |      |         |                |     |         |      |         |            |     |         |      |         | TUNEL + cells per surface unit |     |         |      |         |
|--------|------------------------|-----|---------|------|---------|----------------|-----|---------|------|---------|------------|-----|---------|------|---------|--------------------------------|-----|---------|------|---------|
|        | Epithelial area        |     |         |      |         | Dental papilla |     |         |      |         | Tooth germ |     |         |      |         | Dental papilla                 |     |         |      |         |
|        | Control                |     | 100-CPA |      |         | Control        |     | 100-CPA |      |         | Control    |     | 100-CPA |      |         | Control                        |     | 100-CPA |      |         |
| Age    | mean                   | SD  | mean    | SD   | p-value | mean           | SD  | mean    | SD   | p-value | mean       | SD  | mean    | SD   | p-value | mean                           | SD  | mean    | SD   | p-value |
| Day6.5 | 7.0                    | 4.0 | 23.7    | 16.2 | 0.06699 | 1.5            | 1.5 | 5.2     | 3.1  | 0.03986 | 8.5        | 4.4 | 28.8    | 18.1 | 0.05051 | 0.3                            | 0.5 | 0.5     | 1.1  | 0.76767 |
| Day7   | 8.7                    | 8.7 | 48.2    | 15.4 | 0.00054 | 0.2            | 0.4 | 22.5    | 5.6  | 0.00030 | 8.8        | 8.6 | 70.7    | 20.4 | 0.00042 | 0.0                            | 0.0 | 19.0    | 5.2  | 0.00046 |
| Day8   | 4.2                    | 2.8 | 74.0    | 19.6 | 0.00053 | 1.7            | 2.1 | 47.7    | 13.3 | 0.00060 | 5.8        | 3.3 | 121.7   | 29.9 | 0.00035 | 0.5                            | 0.8 | 27.3    | 13.6 | 0.00693 |
| Day10  | 3.2                    | 3.1 | 9.8     | 5.6  | 0.04072 | 0.2            | 0.4 | 4.7     | 5.0  | 0.05024 | 3.3        | 3.0 | 14.5    | 1.0  | 0.00637 | 0.3                            | 0.5 | 7.2     | 3.4  | 0.00698 |