

## TESTICULAR TISSUE FREEZING: IMPACT OF THE FREEZING PROCEDURE AND THE TREATMENT RECEIVED ON THE QUALITY OF THE TISSUE AFTER THAWING

Rives, Aurélie<sup>1</sup>; Liard, Agnès<sup>2</sup>; Mitchell, Valérie<sup>3</sup>; Bubenheim, Michael<sup>4</sup>; Mirallié, Sophie<sup>5</sup>; Giscard d'Estaing, Sandrine<sup>6</sup>; Roux, Christophe<sup>7</sup>; Benhaim, Annie<sup>8</sup>; Brugnon, Florence<sup>9</sup>; Daudin, Myriam<sup>10</sup>; Schneider, Pascale<sup>11</sup>; Bironneau, Amandine<sup>12</sup>; Rives, Nathalie<sup>13</sup>

<sup>1</sup>EA 4308 Gametogenesis and Gamete Quality Reproductive Biology Laboratory Rouen University Hospital, <sup>2</sup>Chirurgie infantile, CHU de Rouen Normandie, <sup>3</sup>EA 4308 Gametogenesis and gamete Quality Laboratoire de Spermiologie-CECOS, CHRU de Lille 2, Université de Lille 2, <sup>4</sup>DRCI CHU de Rouen Normandie, <sup>5</sup>CECOS Nantes CHU de Nantes, <sup>6</sup>CECOS de Lyon CHU de Lyon, <sup>7</sup>Laboratoire de Biologie de la Reproduction CHU de Besançon, <sup>8</sup>Laboratoire de Biologie de la Reproduction CECOS de Caen CHU de Caen, <sup>9</sup>CECOS Auvergne CHU de Clermont Ferrand, <sup>10</sup>CECOS Toulouse CHU de Toulouse, <sup>11</sup>IHOP CHU de Rouen, <sup>12</sup>EA 4308 Gametogenesis and Gamete Quality Reproductive Biology Laboratory Rouen University Hospital, <sup>13</sup>EA 4308 "Gametogenesis and Gamete Quality" Reproductive Biology Laboratory Rouen University Hospital

### Abstract Body

**Introduction.** In pre-pubertal boys with cancer, infertility caused by treatments has been ignored for a long time, surgical removal of testicular tissue and its freezing is one of the possible procedures to preserve their fertility. The aim of this study was to determine the impact of (i) the freezing procedure on the seminiferous tubule architecture and (ii) the pathology or the cancer treatment received prior to testicular tissue cryopreservation on the number of spermatogonia present in seminiferous tubules.

**Materials and methods.** The study population included boys with cancer aged between 1 and 16 years before conditioning treatment for hematopoietic stem cell transplantation within the context of cancer and after receiving low gonadotoxic treatment. Histological analysis was performed on testicular biopsies before and after freezing. Immuno-histological markers were used to assess the number of spermatogonia (MAGE-A4) and their proliferative ability (PCNA). The histological changes induced by the freezing procedure, the pathology or the associated treatments were evaluated. **Results.** A total of 91 patients (mean age : 7±4 years) were included with 46% of them with acute leukemia, 48% with solid tumor and 6% with lymphoma. Testicular tissue alteration score increased after thawing ( $p < 0.0001$ ), but remained less than 1, in agreement with a good preservation of the seminiferous tubule architecture. The number of intra-tubular spermatogonia ( $p = 0.6568$ ) and their proliferative ability ( $p = 0.7819$ ) did not vary after thawing. We found a decrease in the number of intra-tubular spermatogonia after gonadotoxic treatment including alkylating agents ( $p = 0.0353$ ) and according to their cumulative dose. **Conclusion.** Alkylating agents have a detrimental systematic effect on spermatogonia number. It would seem advisable to propose testicular tissue preservation, as soon as the chemotherapy protocol includes alkylating agents with a Cyclophosphamide Equivalent Dose > 4000 mg/m<sup>2</sup>.