CRANIO-FACIAL BONE DYSMORPHOLOGIES IN RELATION WITH GENE MUTATIONS SCREENED BY CEPHALOMETRIC TOOL

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INTRODUCTION: Many mutations lead to craniofacial dysmorphologies which are difficult to screen. Whole Mount techniques have been used but they are not as accurate and time consuming. On the other hand, cephalometry is a technique of interpretation of cephalic extremity radiology. It illustrates the relations between bone structures, dento-alveolar processes and dental arches in the 3 directions of space. Therefore, we propose a new technique to screen cranio-facial bone dysmorphologies using a modified cephalometric analysis on profile micrographs to explore the sagittal and vertical directions.

METHODS: A microradiography is a radiography taken under conditions which permit subsequent microscopic examination. One of these conditions is called the X-Ray pin-hole source: the X-ray beam is collimated by a lead diaphragm with a pin-hole. This very small X-ray source allows to limit the half light phenomenon and so to optimize the image. We use high resolution films Kodak SO 343. The microradiographies were digitized with a scanner (EPSON Perfection 1640).
After determination specific points, measurements and shape analysis were done on four month Msx2 mutant animals.

Classical cephalometry analysis on profile microradiographies were used to analyze the craniofacial measurements. The following craniofacial distances and angles were calculated :(1) two craniofacial lengths and two craniofacial heights;(2)The thickness of the upper and lower incisors;(3)the thickness of their periodontal ligament;(4)the dental arch discrepancy which can be evaluated by the distance between the maximum of convexity of the mesial side of the first upper and lower molars to a vertical line lowered from the point of emergence of the mesial root of the first upper molar;(5)the antero-posterior bone basal discrepancy by the difference of those two angles; (6)the cochlear apparitus orientation evaluated by the angle between the highest point of the Internal Acousticus Meatus, the highest point of the External Acousticus Meatus and the infraorbital foramen

Shape analysis was done with the PROCUSTE superimpositions. This analysis allows to study and compare the shape of different geometrical figures with different size. Non parametric Wilcoxon test was used to statistical analysis.

RESULTS: Compared to the wild type and the Msx2 heterozygote's animal, vertical and sagittal cranio facial measurements showed that the msx2-/- mutant presents :(1) a smaller size ($p<0,05$), (2) a larger bone basis discrepancy ($p<0,05$), (3) a larger dental arches discrepancy ($p<0,05$), (4) a smaller thickness of the inferior incisor ($p<0,05$), (5) a larger thickness of the periodontal ligament ($p<0,05$) and (6) a clock direction rotation of the cochlear apparatus ($p<0,05$).
Compared to the wild type and the Msx2 heterozygote's animal the shape analysis showed (1) an overall craniofacial shape significantly different ($p<0,01$) and (2) a upper incisor shape with an inferior curvature ($p<0,01$)

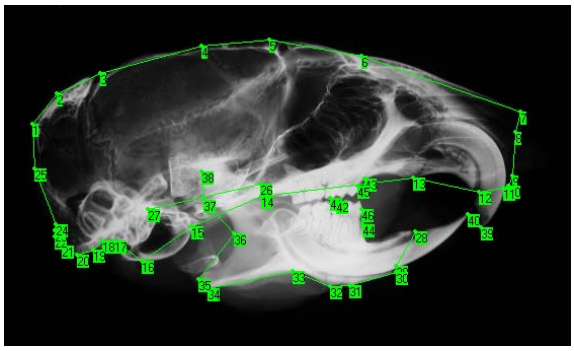

Fig. 1: 46 points have been chosen to characterize the dimensions and the shape of the head.

DISCUSSION & CONCLUSIONS: Classical cephalometry and PROCUSTE superimpositions applied to profile micrographs revealed to be an accurate and simple tool to screen cranio-facial dysmoprphlogies. A 3D cranio-facial bone dysmorphologies study is in process using a micro-computed tomography system (desktop Sky scan 1072) coupled to cephalometry analysis allowing 3D investigation of the whole mice head in relation with gene mutations.