
Poster No.: C-1242
Congress: ECR 2012
Type: Scientific Exhibit
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Keywords: Paediatric, Ear / Nose / Throat, Computer applications, CAD, CT, Image manipulation / Reconstruction, Computer Applications-3D, Computer Applications-General, Segmentation, Congenital
DOI: 10.1594/ecr2012/C-1242

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Isolated Pierre Robin Sequence (IPRS) is characterized by severe micro- or retrognathia, glossoptosis, respiratory obstruction, and a cleft palate. Depending on the severity of IPRS, surgery may be indicated to repair the cleft palate, protect the airway, aid in feeding and especially to improve breathing. Even if an underdeveloped lower jaw is a common finding in these patients, it's likewise true that the underdeveloped lower jaw will grow out on its own during the first two years in many cases. For this reason most authors suggest to treat mild cases with just prone positioning (eventually using special "sniffing air" beds) while tracheostomy (TS) will be necessary for those patients with severe subglottics obstructions. The dispute is still wide open about the gold standard treatment for the remaining part of patients with IPRS (which account for about 20%). For these patients there are four major treatment options: nasopharyngeal airway (NP airway, NPA), tongue-lip adhesion (TLA), floor-of-mouth release (FoMR), and distraction osteogenesis (DO): all these procedures, as well as TS, has a severe impairment on everyday life and/or significant morbility. Since IPRS is so heterogeneous and rare there is no agreement about the use of a conservative approach instead of a more aggressive one: up to today there is no absolute indication to surgery. Some Authors suggest that PRS should be treated, in children and adults, with mandibular DO because that it is the only treatment that really addresses the problem of the small lower jaw.

Aware that many other studies are needed to better understand the pathogenesis and evolution of this disease, hence we suggest an automated, computer assisted, tool to assess the reduction of upper airways calibre by the use of an homemade script applied to the images obtained by the use of multidetector computed tomography (MDCT).
Methods and Materials

Between January 2007 and April 2008, 5 patients with isolated PRS confirmed on both clinical evaluation and by laboratories tests (3 males, 2 female, mean age 49.8 days) and 3 controls not affected by cranio-facial anomalies but with similar age, sex and weight, underwent to a cranio-facial and neck MDCT study (BrightSpeed 16 GE Heathcare). The 5 patients with PRS underwent to MDCT examination for a preliminary evaluation of upper airways calibre; the 3 controls underwent to MDCT examination for different clinical questions. MDCT scans where performed with the following specifications: 120 Kvp, 100 mAs, slice thickness 1.25mm (pixel spacing 0.484375mm), matrix size 512x512 pixels, mean number of slices analysed 60. Datasets obtained from the MDCT studies where than processed with the homemade script compiled in MATLAB (Natick, Massachusetts: The MathWorks Inc.) to automatically calculate the volume of upper airways and easily obtain three dimensional volume rendering (3D-VR) reconstructions with the aim to correlate the results with indication for surgery.

The segmentation algorithm we used is based on a dynamic region growing procedure that exploits the different density of anatomical structures, which result in a strong brightness contrast between upper airways and the surrounding tissues. This algorithm showed great performances in term of accuracy due to the intrinsic difference in density of the structures examined.

ROI Segmentation: a region-growing algorithm starting from a seed-point selected by the operator by mouse-clicking the structure of interest was used for the segmentation and the extraction of the ROI. The algorithm extracts the selected ROI with excellent results. This technique is even better than those based on the classical global thresholding since it doesn't need the user to highlight areas of interest.

The region-growing algorithm allows to easily select pixels that have "affinity" (in terms of brightness or darkness) with the given seed-point (Fig.1); the second step is the segmentation of a ROI (Fig.2); at the end of the segmentation procedure, an edge-detection algorithm allows to extract ROI contours (Fig.3) thus obtaining the data necessary for volumetric reconstructions of the analysed airways.

Obviously, the post-processing is slightly more complex in cases with PRS: since these patients usually have a laryngo-esophageal stenosis and/or an irregular section and morphology of these anatomical channels, the region-growing algorithm, would not always find it's way for a good segmentation. This may lead the algorithm to the extraction of a ROI beyond the area of interest. For these cases a variant of the region-growing algorithm described above was used and this allowed a more precise segmentation by asking the user to select just two points of the slices: the first one inside the ROI and the second one on the surrounding tissues.
3D Volume Rendering (3DVR) reconstructions: as we told, ROI segmentation was also used for 3D-VR reconstructions which allow a panoramic view of the laryngo-pharyngeal tract's morphology and provide useful information for both the assessment of severity and surgical planning (Fig 4, 5: control patient without PRS; Fig. 6, 7 patients with PRS). ROI's edges extraction applied to all slices is followed by three main post-processing steps that will lead to 3D-VR reconstructions. The first one is the isosurface extraction from the dataset (isosurface is calculated from the extracted edges obtained from the previous region-growing and edge-detection operations). The second one is the creation of a set of polygons (triangles) for a better approximation of the isosurface previously built. A third step is needed to calculate the surface normal to the extracted isosurface to achieve a blunter surface, avoiding thus the "edginess" of the polygons-based surface. This optional step is needed to increase the visual quality of the final rendering by adding some virtual light sources.
Images for this section:

**Fig. 1:** The region-growing algorithm with the select pixels that have "affinity" (in terms of brightness or darkness) with the given seed-point.

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**Fig. 2:** The segmentation of a ROI in Red

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**Fig. 3:** The segmentation procedure, an edge-detection algorithm allows to extract ROI contours.

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**Fig. 4:** 3D Volume Rendering (3DVR) reconstructions in control patient without PRS, a panoramic view of the laryngo-pharyngeal tract's morphology.

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Fig. 5: 3D Volume Rendering (3DVR) reconstructions in control patient without PRS, a panoramic view of the laryngo-pharyngeal tract’s morphology.

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**Fig. 6:** 3D Volume Rendering (3DVR) reconstructions in control patient with PRS, a panoramic view of the laryngo-pharyngeal tract's morphology.

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**Fig. 7:** 3D Volume Rendering (3DVR) reconstructions in control patient with PRS, a panoramic view of the laryngo-pharyngeal tract's morphology.
Results

The data collected from patients without PRS revealed a regular pattern with an appreciable calibre of the laryngo-pharyngeal tract with a mean cross sectional area (CSA) of 5.1cm², mean variance of 0.276 and a mean volume of 15.45cm³. In patients with PRS, the upper airways showed an irregular pattern and a severe reduced cross section (Fig.2a, b, c, d) with a mean of 1.786cm², mean variance of 8.268 and a mean volume of 2.855cm³. In one case we found a complete severe stenosis of the air duct (Fig2.d) but in all cases with PRS we found a significant lower mean CSA (about 34.67% of controls) and mean volume (about 18.47% of controls) and significant higher mean variance value of segmented ROI.
Conclusion

PRS is a rather uncommon craniofacial condition that may lead to severe constriction of the upper airways. The possibility of measuring the volume of the upper airway to select patients eligible for surgery may be decisive for patients' outcome; our preliminary results seems to meet the requirements for this kind of evaluation: the developed algorithm can be integrated in a useful Decision Support System and used as an automatic clustering method. Our algorithm however is not free from drawbacks.

The main limitation of our method depends on breathing: to avoid general anaesthesia and or tracheal intubation, these patients are usually subjected only to a mild sedation and so the CT studies are not acquired with a respiratory synchronized protocol. This can results in a considerable variability of upper airways calibre on each single patient that may lead to inaccurate data of the actual patients' airways volume. Acquiring CT studies of these patients using only a mild sedation can also occur on bad datasets due to the presence of patient-based artefacts mainly caused by patient's movement. However, these kinds of restrictions/limits are to be considered intrinsic to the current state of CT studies in non-intubated paediatric patients.

The second mayor limit of our study is the sample population. But even if our population was pretty small it should be also considered the low incidence of PRS with severe respiratory impairment: our study should to be considered a proof of concept. The only way to avoid this limit is to include our algorithm in a multicentre investigation to obtain more robust statistical significance of the results obtained with the present work.
References


