**Abstracts**

**Diagnosis, Epidemiology and Immune Disturbances**

### 3.1

**Natural History of Splenomegaly in CLL from Automated Volumetric Analysis**

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**Introduction:** We have developed a technique for the automated segmentation and quantification of spleens from contrast-enhanced CT scan data. This technique was applied to a series of CT scans obtained from CLL patients enrolled in a natural history protocol at the NHLBI NIH to better understand the natural history of splenomegaly in CLL.

**Methods and Materials:** Forty-three abdominal CT sets from 22 patients (13 males and 9 females) with CLL were acquired with/out IV contrast on a variety of scanners between 2000 and 2011. In addition to baseline CT scans, 12 patients had between 1 and 3 CT scans prior to treatment. The time interval between consecutive scans varied between 3 and 58 months. Images were acquired at either non-contrast, arterial or portal venous phases.

When IV contrast was used, patients were administered Isovue 300 and the contrast-enhanced data were acquired using either fixed delays or bolus tracking. The image matrix was $512 \times 512$ pixels with sub-millimeter resolution in the axial slice and 5 to 10 mm slice thickness. For the validation of the segmentation technique, 14 additional cases (7 with normal spleens and 7 with splenomegaly) were used with similar acquisition parameters. The 14 cases were acquired at portal venous enhancement with 5 mm slice thickness and their spleens were manually segmented. The spleens were automatically segmented using a probabilistic atlas and non-linear registration. The organ locations were modeled in the physical space and normalized to the position of an anatomical landmark, the xiphoid process. The construction and exploitation of the spleen atlas enabled the automated quantifications of spleen volumes and cephalo-caudal lengths from abdominal CT data. The quantification was improved incrementally by a geodesic active contour, patient specific contrast-enhancement characteristics, and constraints for shape and location.

**Results:** The spleens were robustly segmented from normal and pathological cases. The spleen quantification led to 0.94 symmetric volume overlap, 4.3/3.7% volume/length errors, 2.1 mm root mean square error and 1.3 mm average surface error. The correlation ($R^2$) between automated and manual measurements was 0.98 ($p < 0.001$). The correlation ($R^2$) between automated splenic lengths and volumes was 0.71 ($p = 0.007$). The average splenic volume and length at baseline of all patients ($n = 22$) was $642.72 \pm 353.82 \text{ cm}^3$ and $13.46 \pm 3.52 \text{ cm}$ respectively. For the 12 patients with multiple time points, the average splenic volume and length changed from $724.06 \pm 305.77 \text{ cm}^3$ and $14.52 \pm 3.49 \text{ cm}$ at baseline to $1116.08 \pm 541.37 \text{ cm}^3$ and $17.96 \pm 4.20 \text{ cm}$ before starting treatment. There were statistically significant differences between the volumes ($p < 0.001$) and heights ($p < 0.001$) of spleens measured at baseline and before treatment. Of the 12 patients, 11 exhibited substantial increases in spleen volume, while 1 outlier showed a natural decrease. Consensus literature values for maximum spleen volume and length of normal individuals varies from 290 to 380 cm$^3$ and from 9.8 to 12.0 cm respectively. Using a splenic volume cutoff of 380 cm$^3$ to detect splenomegaly, 70% of all cases and 79% of the patients with multiple time points had abnormal spleens at baseline. 100% of the patients with multiple time points exhibited splenomegaly before the start of treatment. On average, splenic volume increased by 4.74 ± 5.23% every 3 months (5.40 ± 4.43% without the outlier). Using a splenic cephalo-caudal length cutoff of 12 cm to detect splenomegaly, 59% of all cases and 75% of the patients with multiple time points had abnormal spleens at baseline. 100% of the patients with multiple time points exhibited splenomegaly before the start of treatment.

**Conclusion:** The automated method for spleen analysis allows the non-invasive measurement of splenic volume from contrast-enhanced CT data. Automated computer-aided analysis of spleen data in CLL suggests that spleen volume is increased in several patients before it can be physically palpated. It remains to be seen if such subclinical splenic enlargement is associated with early thrombocytopenia. It is envisioned that an automated, standardized analysis would eventually be able to estimate spleen, liver and lymph node volume and yield a 3-dimensional, cross-sectional atlas of the distribution of the disease.