DIGITAL PATHOLOGY IMAGE ANALYSIS APPROACH TO MEASURE THE EXTENT OF KIDNEY FIBROSIS: COMPARISON OF MASSON TRICHROME AND PICRO SIRIUS STAININGS

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Introduction. The extent of kidney fibrosis is widely used as a measure of chronic disease in both native and transplanted kidney biopsies. Semi-quantitative visual evaluation of fibrosis area stained by Masson Trichrome (MS) is widely accepted method. However, MS may underestimate the fibrosis levels, since MS and Picro Sirius (PS) stain different types of collagen. Both staining methods can be in general compared by visual evaluation of pathologist, but more precise comparison may be enabled by digital image analysis(DIA).

Aim. We aimed to compare MS and PS stainings for kidney fibrosis evaluation by DIA.

Methods. Consecutive sections of 59 renal(native and allograft) biopsies were stained by MS and PS, scanned by Aperio XT. Colocalization algorithms were set up to detect fibrous tissue stained by PS and MS. Aperio Genie tool was trained to automatically outline biopsy sections. The Genie tool was connected with each version of Colocalization algorithm. The renal cortex and medulla were analyzed separately based on manual annotations.

No attempt was made to exclude glomeruli or arteries from the analysis for the sake of simplicity and based on an observation that normal and even sclerosed structures do not reveal significant amount of fibrous tissue detected by the DIA tool. Therefore, we measured total cortical fibrosis, rather than pure interstitial fibrosis.

The versions of Colocalization algorithms detected not only fibrosis, but also other structural parts of kidney biopsy: nuclei, glass (liquid), cytoplasm, and basal membranes. The following variables were analysed:patologist_VE, fibrosis_MS, fibrosis_PS, Cytoplasm_PS, cytoplasm_MS, nuclei_MS, nuclei_PS, basal_membrane_MS, basal_membrane_PS, glass_PS, glass_MS. The results of cortex were only used. Factor analysis was performed to explore potential intrinsic factors of the variability in the data set.

Results. Evaluation of normality led to natural log transformation of results. Principal component analysis was conducted utilazing a varimax rotation. The initial analysis retained 3 factors (Eigenvalue >1, factor1=3,03; factor2=1.86; factor3=1.42;). Kaiser‘s measure of sampling adequacy was equal to 0,55(>0,5). The glass_MS and glass_PS were excluded because of low correlation with other variables(<0,3). The first component included items with both negative(cytoplasm_PS=-0,92) and positive(fibrosis_PS=0,78;fibrosis_VE=0,78) loadings. Second component included items with both negative(cytoplasm_MS=-0,81) and positive(nuclei_MS=0,90,nuclei_PS=0,50) loadings. Third component included items with negative (fibrosis_MS=-0,77) and positive (basal_membrane_MS=0,87) loadings.

Conclusions. Our DIA approach was designed to compare the fibrotic tissue estimates by MS and PS stainings. The factor 1 was characterised by positive loadings of Pathologist‘s VE and extent of fibrosis by PS but not MS stain. It can be interpreted that in biopsy diagnosis, the pathologist tended to evaluate irreversible changes in kidney biopsy and relied

more on interstitial expansion reflected better by PS rather than MS stain. The fibrosis extent by MS had different loads in 2 and 3 factors, potentially reflecting technical instability and/or biological variation of fibrosis containing different collagen types by MS staining.