Measurement of Glomerular Filtration Rate using Quantitative SPECT/CT and Deep-Learning based Kidney Segmentation

Abstract

- Quantitative SPECT/CT : useful for accurate and reliable measurement of GFR
    - Manual drawing of VOI in CT images : labor-intensive & time consuming

$\Rightarrow$ Aim of this study : develop fully automated GFR quantification method based on deep-learning approach to the 3D segmentation of kidney parenchyma in CT

- Proposed method
    - High Dice similarity coefficient (mean = 0.89)
    - Strongly correlated GFR (R2 = 0.96)
    - Absolute difference : 2.90%
    - Comparable performance in urolithiasis patients and kidney donors
    - Decrease individual GFR in symptomatic kidney vs normal
    - Fast and accurate GFR measurement

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Introduction

- GFR : a flow rate of blood plasma which is filtered through glomerulus

- Kidney SPECT/CT with $^{99m}Tc - DTPA$: method for measurement of GFR
  - Quantitative and reliable in measuring the renal clearance
  - VOI : drawn on each kidney for the quantification of absolute radioactivity
  - → necessity of manual drawing of VOI on the whole renal parenchyma in CT images
    - → Labor intensive, time consuming(take 15 min per scan)

- Aim of this study : develop automated GFR quantification method
  - Based on deep learning approach to 3D segmentation of kidney parenchyma in CT

- GFR quantification : need segmentation of the only functioning kidney parenchyma
  - → deep CNN to learn end to end mapping between 3D CT volume and manually segmented VOI by experts
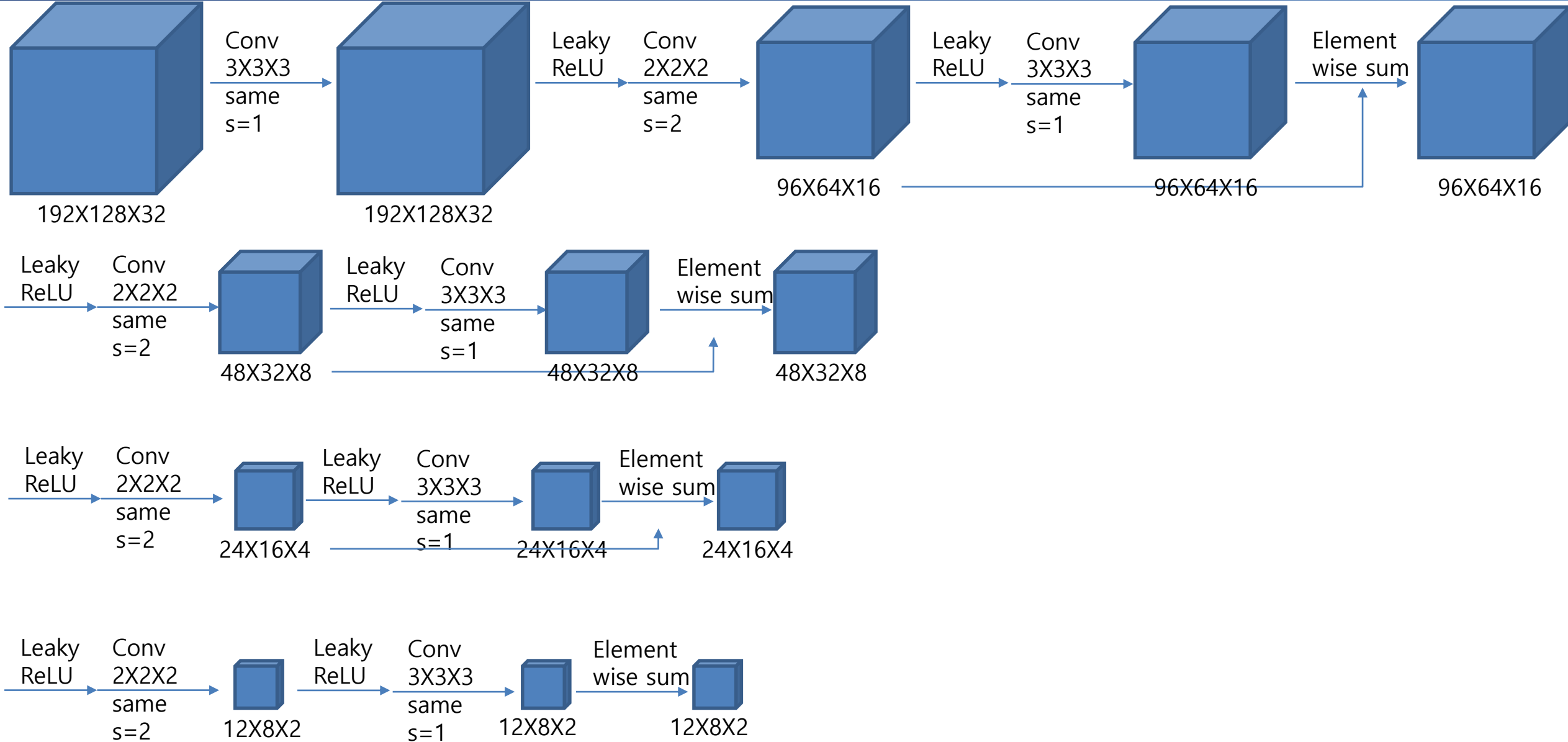
Method - dataset

- Data : $^{99m}Tc - DTPA$ kidney SPECT/CT data of 393 patients – training/validation

- Physician draw ROI -> automatic interpolation(by software) => exclude unwanted structure

- Quantitative kidney SPECT/CT : perform **without iodine-contrast enhancement**
  - Renal tumor patients : remained iodine contrast enhancement (22.6%)

1. Resampling to have same matrix for training : 256 X 256 X 232, $1.726mm^3$

2. Crop image to reduce memory consumption : 192 X 128 X 96
   - Large enough to include both kidneys

3. Apply 3D volume smoothing & morphological operation to manual VOIs
   - Reduce discontinuity in 3D space

Method – Neural Network architecture

- Use modified 3D U-net
  - End to end mapping between 3D - CT and manually drawn renal parenchyma VOIs

- Contraction path : capture the context
  - 5 sequential layers
  - 3X3X3 conv → leaky ReLU → 2X2X2 strided conv → leaky ReLU → 3X3X3 conv → elementwise sum

  Pre-activation residual block

- Expansion path : enable precise localization
  - 5 sequential layers
  - Upsampling : 1X1X1 conv → leaky ReLU → 2X2X2 deconv → leaky ReLU → 3X3X3 conv → leaky ReLU
  - Employ symmetric skip connection

- Use 3D spatial drop-out(rate 0.3)
  - Adjacent voxels : correlated compared with batch normalization

Method – Neural Network architecture
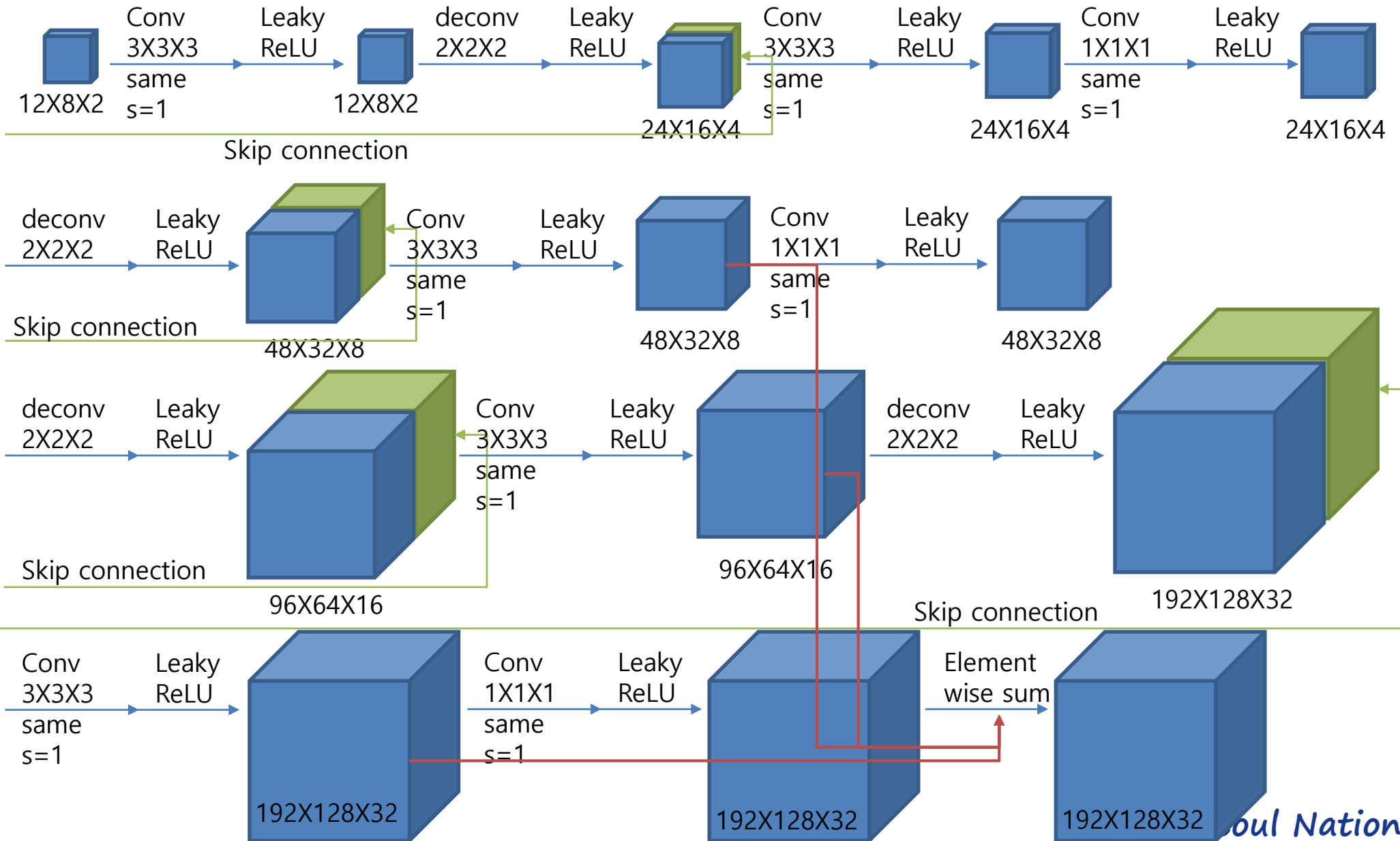
Method – Network Training/GFR estimation

- Training set : 315 patients / Validation set : 78 patients (randomly select)

- Input / Output dataset : 3D volume format

- Loss function : dice similarity coefficient

- Optimizer : Adam (β_1 : 0.9, β_2 : 0.999, ϵ : 0)

- Learning rate : 0.0005 (reduced by half after 10 epochs if loss function not improve)

- Epoch : 80 (each epoch – 272 iterations)

- $GFR(ml/min) = (\%id \times 9.1462) + 23.0653$
  - %id : calculated by applying the manual and automatic VOIs

- $Total\ GFR(ml/min/1.73m^2) = GFR(ml/min) \times (1.73/BSAm^2)$
  - $BSAm^2 = 0.007184 \times (weight\ in\ kg)^{0.425} \times (height\ in\ cm)^{0.725}$

Method – Further Validation

- Patients with urinary stones & kidney donors as negative controls
  - 126 kidneys from 63 urinary stone patients (age higher than normal group)
  - 50 kidneys from 25 kidney donors
  - ⇒ 50 normal kidneys (from kidney donor patients)

    48 symptomatic kidneys (either ureter stone of any size or large renal stone/longest diameter>10mm)

    78 asymptomatic kidneys (either small renal stone or contralateral kidney

- GFR value for manual segmentation
  - Average of two independent measurement of GFR by four medical experts
- GFR value for automatic segmentation
  - Single measurement of GFR

Method – Data Analysis

- Evaluation : calculate Dice similarity coefficient
  - Assess correlation, mean absolute percentage error
- Perform 5 – fold cross-validation

- Statistical analysis in urolithiasis patients
  - Evaluate normality of data : use D'Agnostino-Pearson test
  - Parametric : independent samples t-test / one-way analysis of variance
  - Nonparametric : Mann-Whitney test / Wilcoxon test / Kruskal-Wallis test
  - Chi-square test : analysis of categorical data
  - Multiple comparison correction for t-test : Bonferroni correction
 - Results with P-values less than 0.05

Results – Segmentation

- High Dice similarity coefficient : mean $\pm$ SD = 0.89 $\pm$ 0.03

- 3D kidney parenchyma VOIs : no discontinuity between slices (CNN trained to produce smooth 3D VOIs)

- Time requirement : a few seconds per patient
  – Manual segmentation : 15 min per scan

- Ablation study

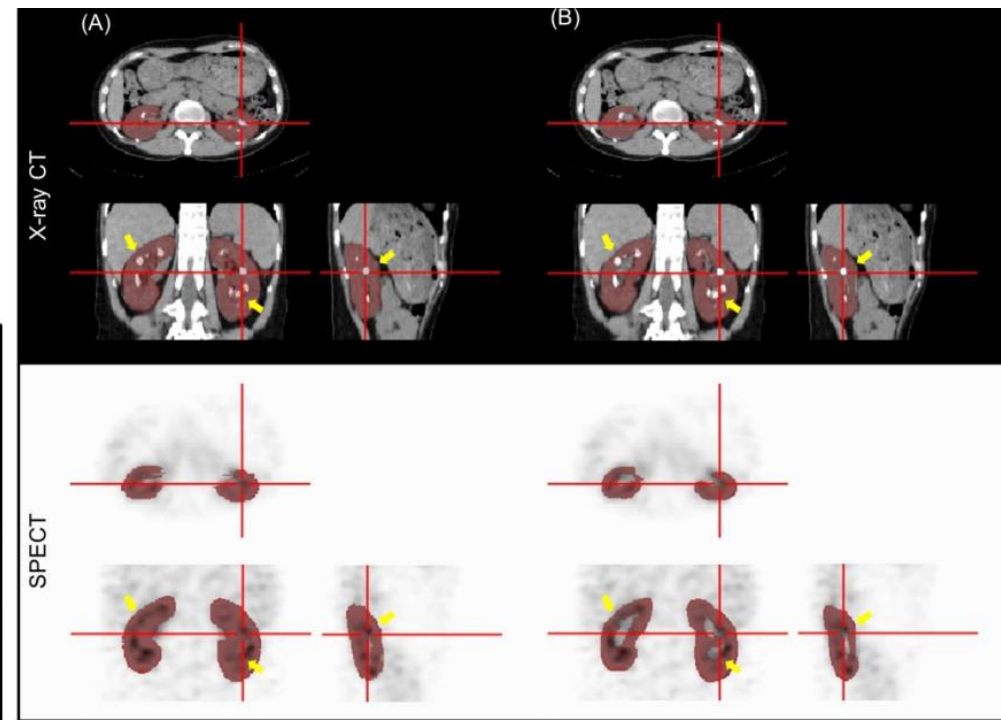| Model	Version	Average Dice Score
3D U-Net	+ Down-sampling (x2) + Batch normalization (batch size = 2)	0.848
	+ Drop-out (P_{drop}* = 0.3)	0.862
	+ Residual block, Element-wise sum array	0.885
	+ Residual block, Element-wise sum array + Drop-out (P_{drop} = 0.3)	**0.890**

* P_{drop}: Drop-out rate

- Result
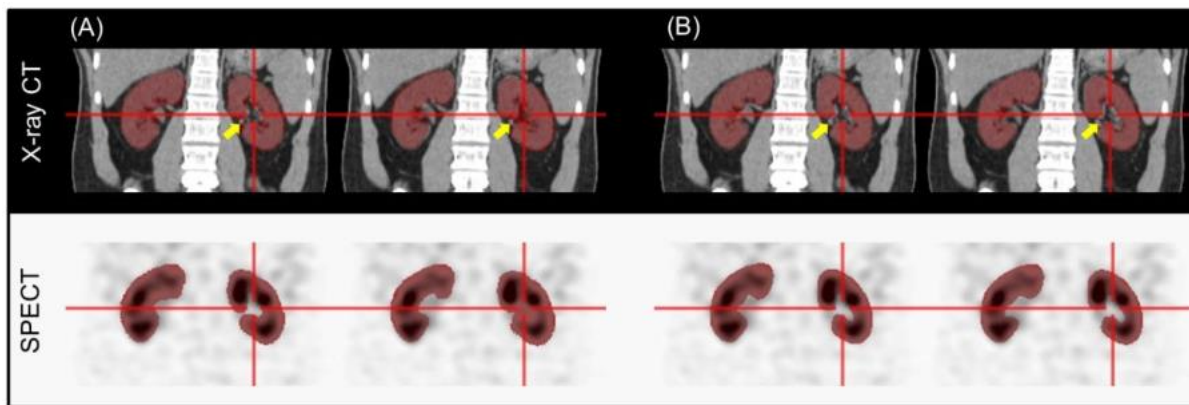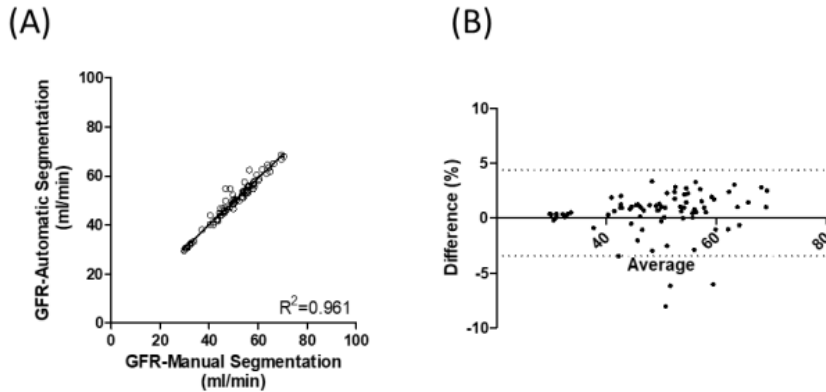

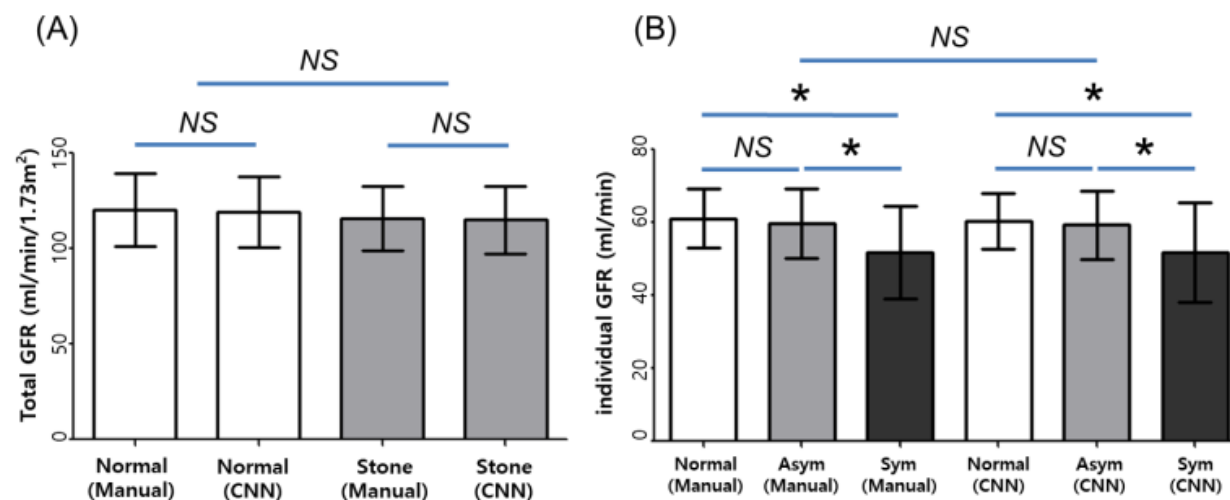manual   segmentation

- GFR value : manual and proposed method - strongly correlated for total kidney - $R^2 = 0.96$
- Scattered(A) and Bland-Altman plots between GFR using manual and deep-learning

- Mean absolute percentage – in all 5-fold cross validation
  - Absolute difference : 2.90 $\pm$ 2.80% (left kidney : 3.12 $\pm$ 2.99 % , right kidney : 3.13 $\pm$ 2.80 %)
- Correlation coefficient R^2 for five sets : 0.95 to 0.96

Results – Validation

- Total GFR_{manual} in kidney donors : 120.39 ± 19.26 ml/min/$1.73m^2$ (P = 0.4432, Wilcoxon test)
- Total GFR_{CNN} in kidney donors : 119.25 ± 18.35ml/min/$1.73m^2$

- Total GFR_{manual} in urinary stone patients : 115.65 ± 16.91ml/min/$1.73m^2$(P = 0.2387, paired t-test)
- Total GFR_{CNN} in urinary stone patients : 115.02 ± 17.71ml/min/$1.73m^2$

- Individual kidney GFR
  - GFR_{manual} : 61.01 ± 8.10ml/min/$1.73m^2$
  - GFR_{CNN} : 60.43 ± 7.66ml/min
- Asymptomatic kidney GFR
  - GFR_{manual} : 59.72 ± 9.46ml/min/$1.73m^2$
  - GFR_{CNN} : 59.23 ± 9.25ml/min/$1.73m^2$
- Symptomatic kidney GFR
  - GFR_{manual} : 51.84 ± 12.73ml/min/$1.73m^2$
 - GFR_{CNN} : 51.76 ± 13.69ml/min/$1.73m^2$

Discussion

- Deep learning approach
  - highly accurate in renal parenchyma segmentation in CT
  - useful for automated measurement of GFR
- Automatically drawing VOIs only on renal parenchyma excluding cysts : several cases were not accurate
  1. Incorrectly included, renal pelvis well excluded
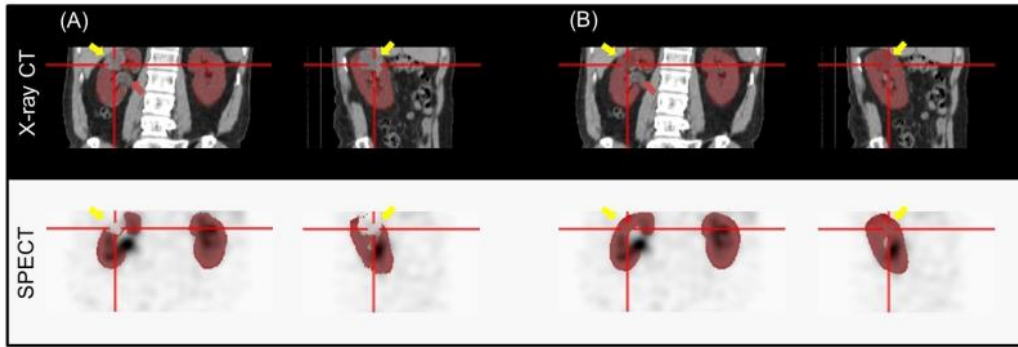
Smaller than others → insufficient data
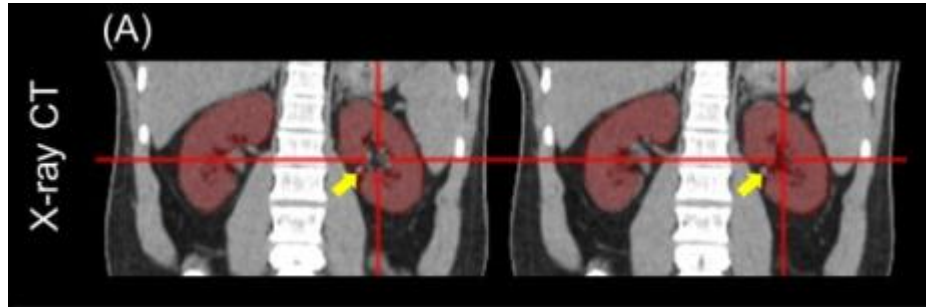⇒ GFR error low (radio activity in tumor very low)

2. Only a single kidney
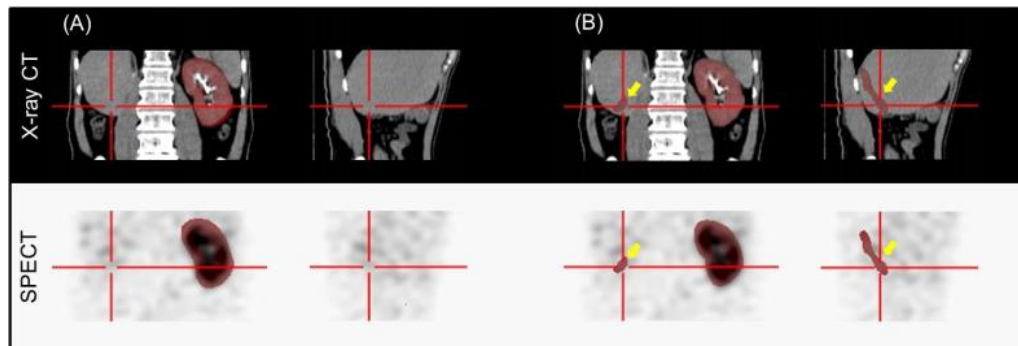
3 single kidney case among training set
⇒ Additional dataset necessary

3. Segmentation error in manual VOIs

Discontinuity in the perpendicular direction to the ROIs
Subsequent inter-slice ROI-interpolation

- Further clinical validation
  - Use in more complicated cases such as multi-cystic dysplastic kidneys