# Heterogeneous Tumor Microenvironment in Non-Small Cell Lung Cancer derived from FDG-PET Data

**Ida R. Jarczyk**
University of Stavanger
ida.r.hansen@uis.no

**Torjan Haslerud**
Stavanger University Hospital;
Haukeland University Hospital

**Geir Nævdal**
NORCE Energy
gena@norceresearch.no

**Steinar Evje**
University of Stavanger
steinar.evje@uis.no

## 1. Introduction

- FDG-PET provides voxel-wise Standard Uptake Value (SUV)
- Standard use: scalar biomarker (metabolic activity)
- **Goal:** Recover underlying tumor properties from SUV
- **Key idea:** Combining:
  - Biophysical porous-media model
  - Transport + reaction of tracer (FDG)
  - Ensemble smoother - multiple data assimilation (ES-MDA)

## 2. Physical Model

Tumor modeled as a two-phase porous medium with cancer cells ($\alpha_c$) and interstitial fluid ($\alpha_w$) and extracellular matrix (ECM) as solid phase

**Key processes:**

- Fluid flow (Darcy-type):

$$
\begin{aligned}
(\alpha_c)_t + \nabla\cdot(\alpha_c \mathbf{u}_c) &= 0\\
(\alpha_w)_t + \nabla\cdot(\alpha_w \mathbf{u}_w) &= Q, \quad Q = Q_v - Q_l\\
\alpha_c \nabla P_c &= -\zeta_c \mathbf{u}_c + \zeta_{cw}(\mathbf{u}_w - \mathbf{u}_c)\\
\alpha_w \nabla P_w &= -\zeta_w \mathbf{u}_w - \zeta_{cw}(\mathbf{u}_w - \mathbf{u}_c)
\end{aligned}
$$

$$
\begin{aligned}
\alpha_c + \alpha_w &= 1\\
P_c &= P_w + \Delta P(\alpha_c) + \Lambda(C)\\
Q_v &= T_v(x)\,(P_v^* - P_w)\\
Q_l &= T_l(x)\,(P_w - P_l^*)
\end{aligned}
$$

- In addition to equations above there are chemical agents influencing tumor progression
- Advection-diffusion of FDG
- Delivery of FDG to interstitial space

$$
\begin{aligned}
d_t + \nabla\cdot(\mathbf{u}_w d) = \nabla\cdot(D_d \nabla d) + \varepsilon^c_{\mathrm{vasc}} Q_v d_v^*\\
+\varepsilon^d_{\mathrm{vasc}} P^* T_v(d_v^* - d) - \lambda_c(\alpha_c + \delta_d) d
\end{aligned}
$$

- Uptake of FDG by cancer cells ($d^c(x,t)$):

$$\frac{d}{dt} d^c(x,t) = \lambda_c\big(\alpha_c d - \delta_d^c d\, d^c\big).$$

- SUV represents final uptake/trapping by cancer cells relatively total injected dose
- FDG is injected and images are acquired approximately 60 min post injection

## 3. Inverse Problem

- We tune the spatial varying fields $\alpha_c^0(x)$, $T_v(x)$, $T_l(x)$ and the parameters $\varepsilon^d_{\mathrm{vasc}} \in [0.1, 1]$, $\varepsilon^c_{\mathrm{vasc}} \in [0, 0.25]$ and $\delta_d \in [0.05, 0.25]$
- Due to lack of information we solve the estimation problem for $\lambda_c = \{0.05, 0.15, 0.30\}$ (low, intermediate and high uptake of FDG) and $k_w = \{1, 4, 16\}$ (low, intermediate, high density of tumor tissue)

## 4. Data assimilation

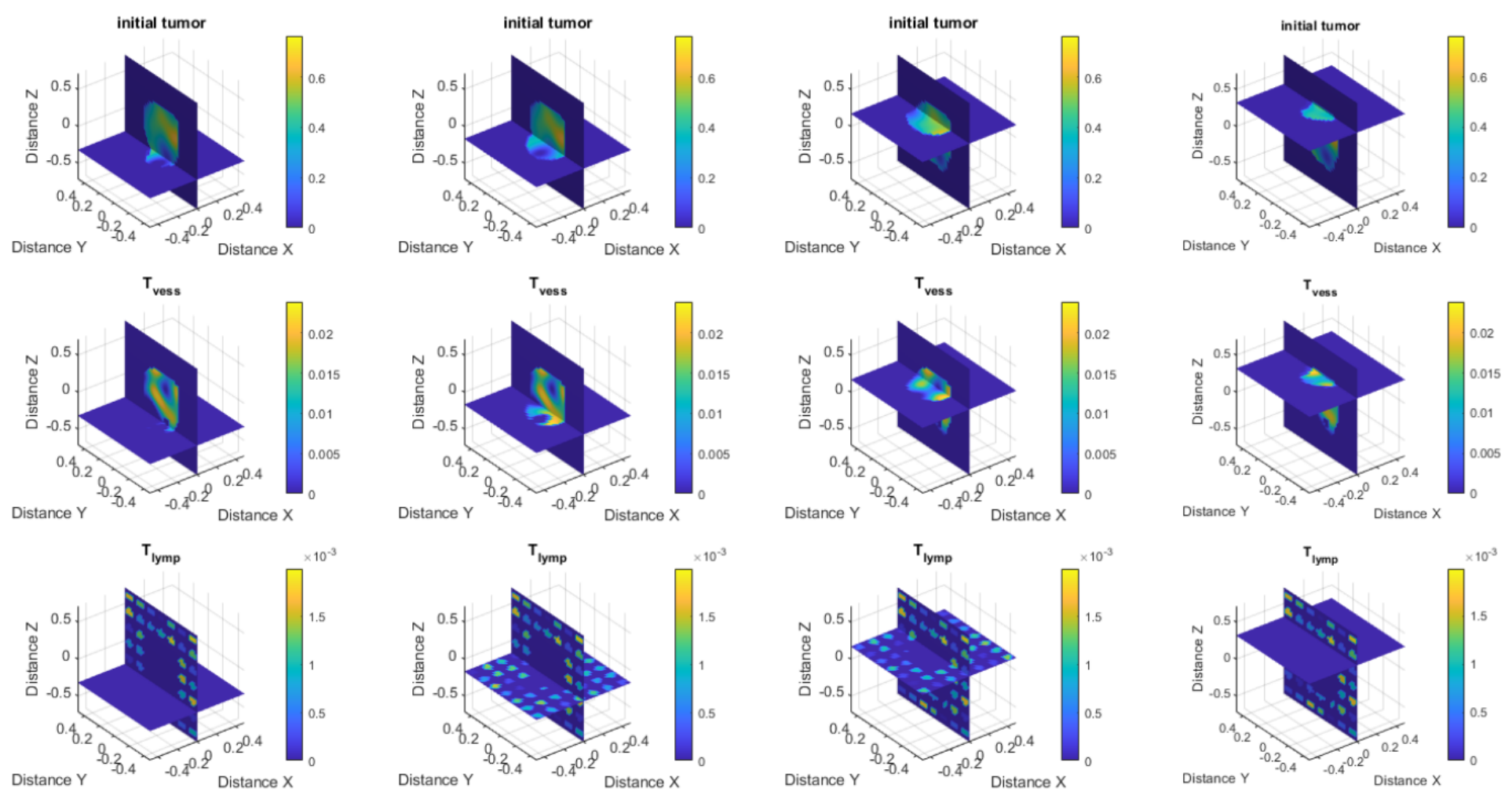
- $Y$: observed SUV (3D field)
- $V = [\alpha_c^0(x), T_v(x), T_l(x), \varepsilon^d_{\mathrm{vasc}}, \varepsilon^c_{\mathrm{vasc}}, \delta_d]$: parameter vector
- $G$: nonlinear forward model
- Cost function

$$J(V) = \frac{1}{2}(Y - G(V))^T \Gamma^{-1} (Y - G(V))$$

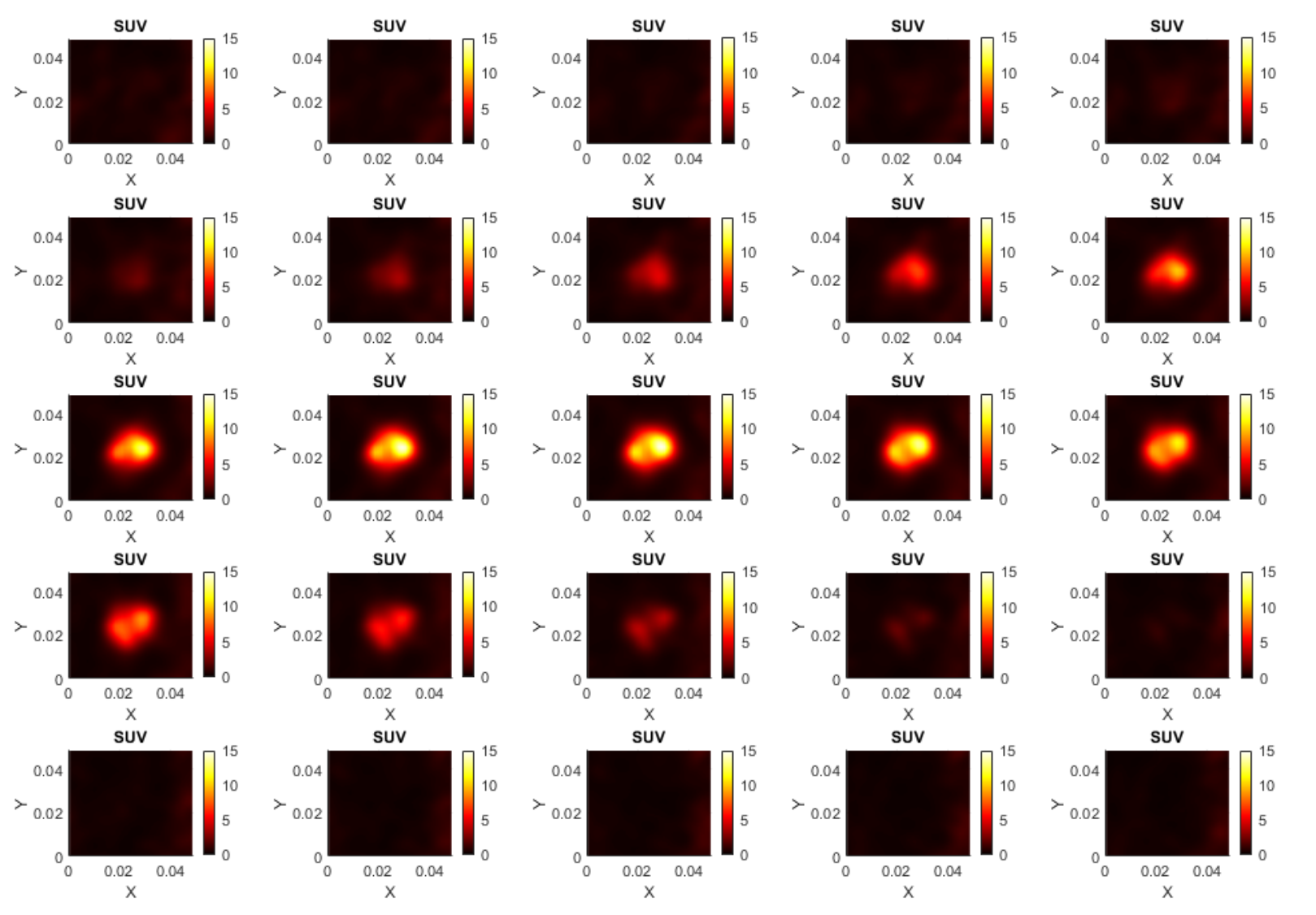
is minimized using ES-MDA with 4 iterations

**Prior distribution:**

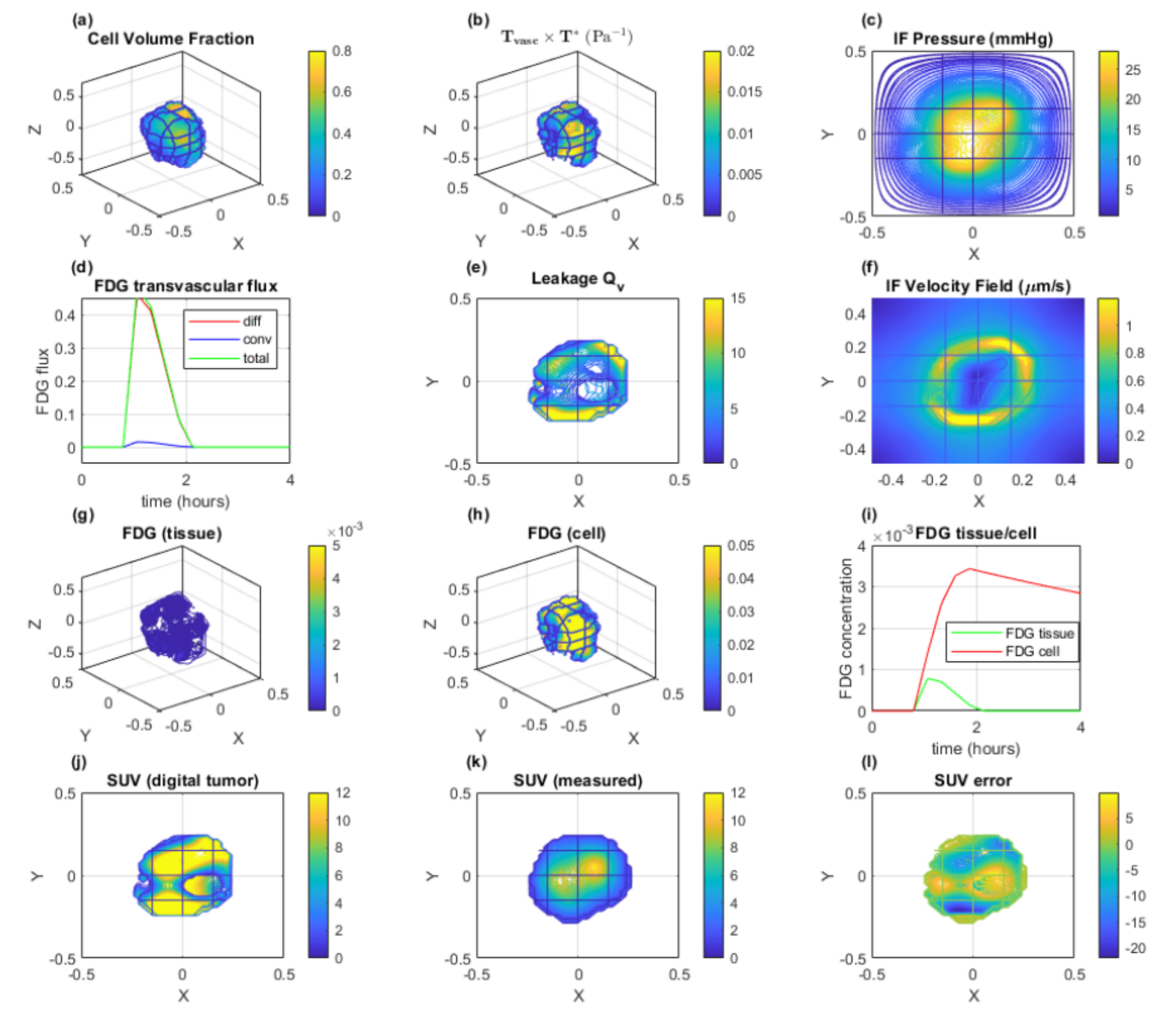
- $\alpha_c^0(x)$ generated using Gaussian variogram
- $T_v(x)$ generated using Gaussian variogram and multiplied by a random factor
- $T_l(x) = T_{l,k} J_k(x)$ where $J_k(x)$ are uniformly distributed "balls" in peritumoral region and $T_{l,k}$ are uniformly distributed
- $\varepsilon^d_{\mathrm{vasc}}$, $\varepsilon^c_{\mathrm{vasc}}$ and $\delta_d$ are uniformly distributed



Initial ensemble member



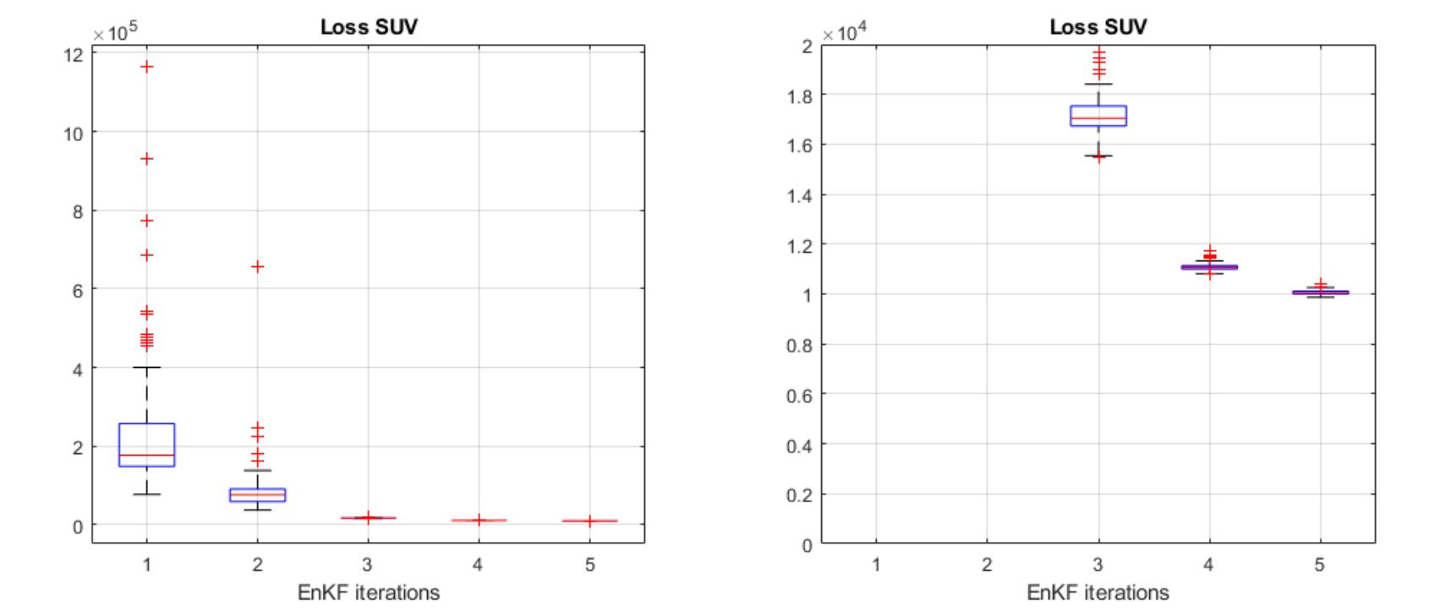
SUV data from patient



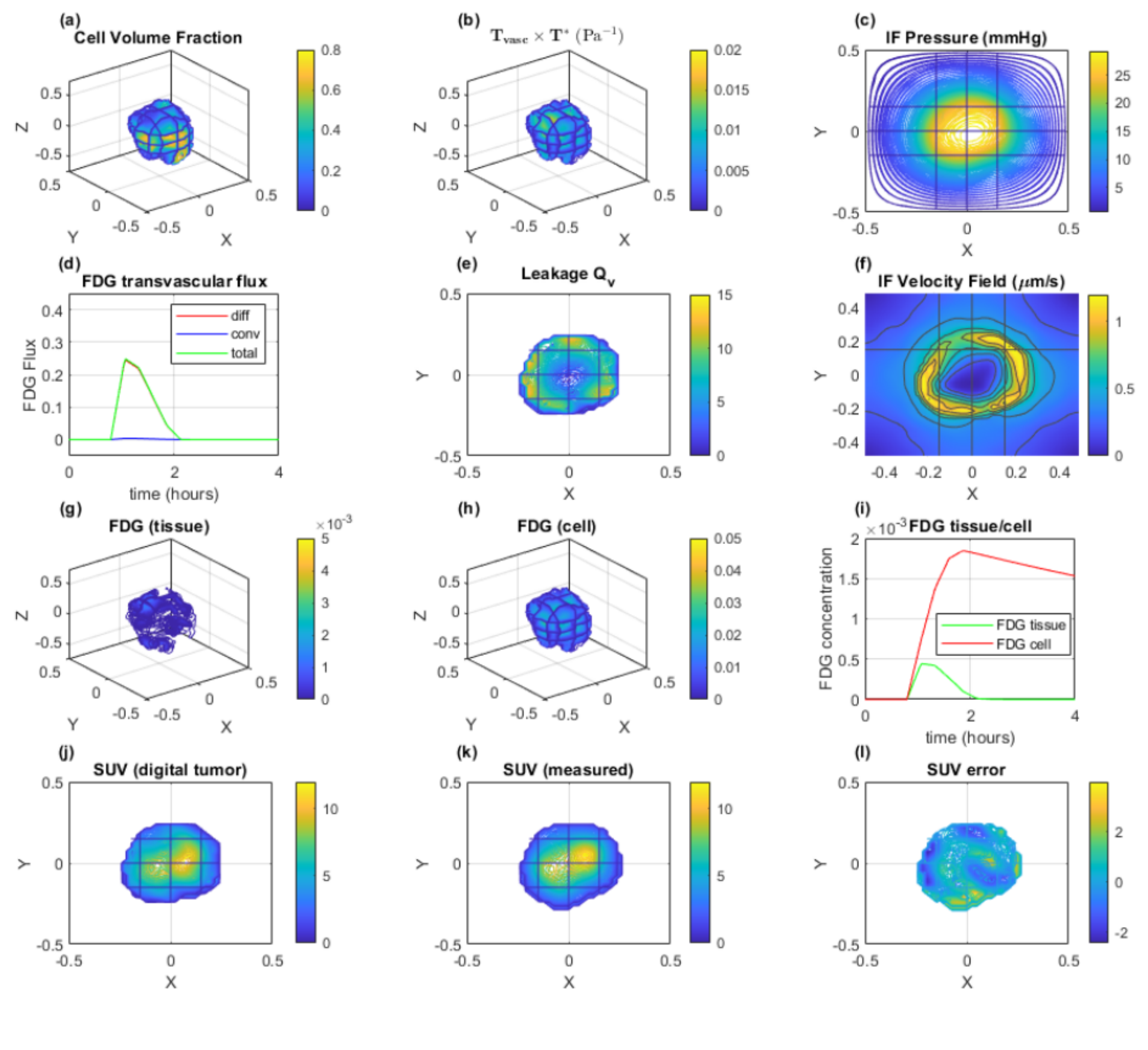
Simulation with an initial ensemble member with $\lambda_c = 0.30$ and $k_w$=1

## 5. Results from data assimilation

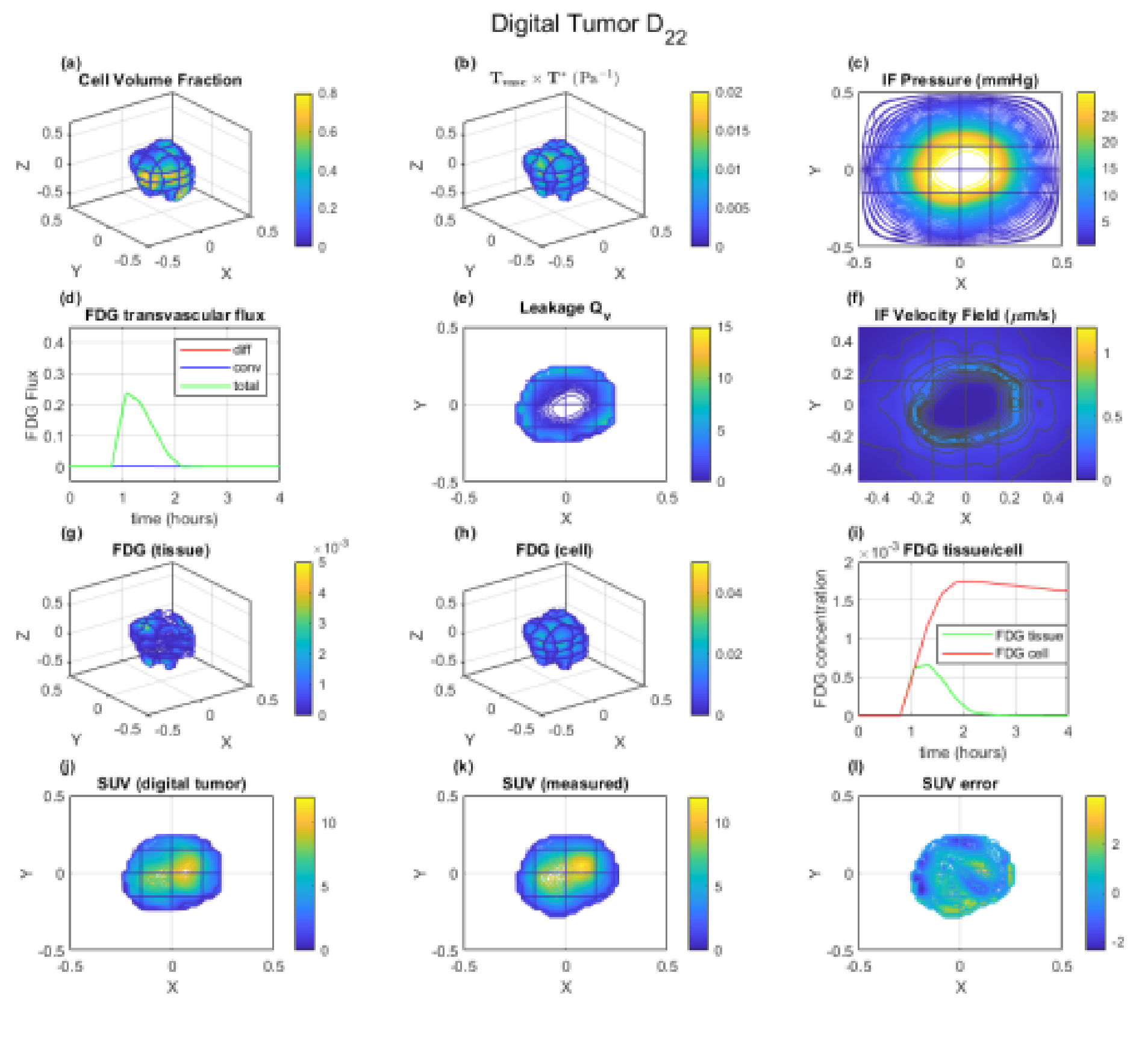
- EnKF reduces mismatch between simulated and observed SUV
- Spatial patterns reproduced after few iterations



Loss function per iteration for the case with $\lambda_c = 0.30$ and $k_w = 1$



Simulation with final ensemble mean with $\lambda_c = 0.30$ and $k_w = 1$



Simulation with final ensemble mean with $\lambda_c = 0.15$ and $k_w = 4$

- Find solutions matching data for all 9 combinations of parameters $\lambda_c$ and $k_w$

## 6. Conclusions

- Find parameter vectors that reproduce SUV data
- Not able to resolve ambiguity with respect to $\lambda_c$ and $k_w$
- Complementary information/data?
- Promising framework for further investigations

NORCE
NORCE Norwegian Research Centre AS
www.norceresearch.no

21th international EnKF workshop (2026)