Functional Data, Covariances and FPCA of Brain Data

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3 February 2016

Acknowledgements

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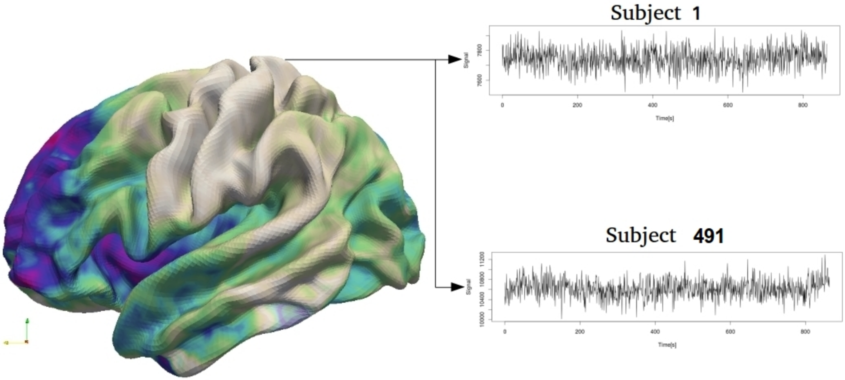
Outline

1. Data and FPCA
2. Aside: FPCA on Surface
3. Mean Stationarity
4. Covariance Stationarity - work in progress

Outline

Data

- Resting state fMRI
- Preprocessing
- Anatomical alignment



Functional Data Model

A model for functional data can be formulated as follows

$$X_i(t) = \mu(t) + Y_i(t), \tag{1}$$

where functional data $\{Y_i(\cdot) : 1 \leq i \leq n\}$ and mean function are elements of $L^2(\mathcal{T})$, where $\mathcal{T}$ is some compact set, and $EY_i(t) = 0$.

A few assumptions and definitions

- The covariance function of $Y_i(\cdot)$ is given by

$$s(t, u) = E(Y_i(t)Y_i(u)).$$

- Let $\{\lambda_k\}$ be the non-negative decreasing sequence of eigenvalues and $\{\phi_k(\cdot) : k \geq 1\}$ a given set of corresponding orthonormal eigenfunctions of the covariance operator, i.e. they are defined by

$$\int s(t, u)\phi_l(u)\, du = \lambda_l \phi_l(t), \quad l = 1, 2, \dots, \quad t \in \mathcal{T}.$$

Functional Principal Component Analysis

- $Y_i(\cdot)$ can then be expressed as

$$Y_i(u) = \sum_{l=1}^{\infty} \eta_{i,l}\phi_l(u),$$

- Further

$$\eta_{i,l} = \int Y_i(u)\phi_l(u)\,du \quad i = 1, \ldots, n, \quad l = 1, 2, \ldots.$$

Resting State fMRI Data

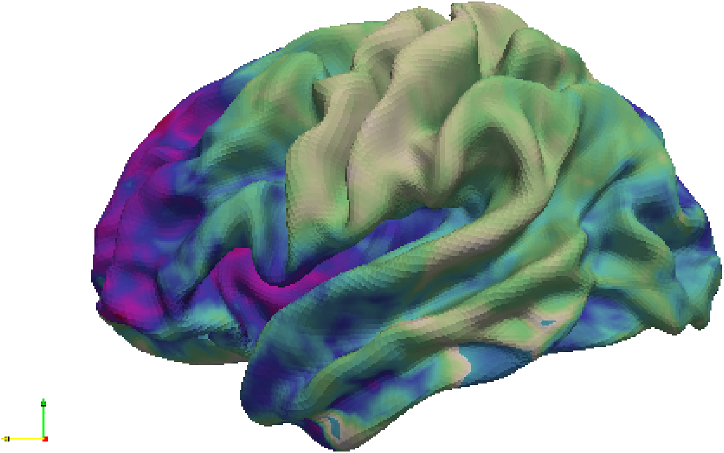
- Lie in a Scanner for several minutes "at rest"
- Used to determine which brain regions are default regions and how they are connected
- Data size approximate $100 \times 100 \times 100$ in space and 200 in time.
- Use separable principal components to find non-stationarities $\Delta(t)$ in the data.

Computational Savings

- Full Covariance $10^6 \times 10^6$ elements to be estimated with 200 samples.
- Separable Covariance $3 \times 10^2 \times 10^2$ elements to be estimated with 200×10^4 samples.
- Sample eigenbasis is 200 dimensional
- Separable sample eigenbasis is 10^6 dimensional.

Outline

The cortical surface



Smooth-Manifold FPCA

Lila et al, arXiv, 2016

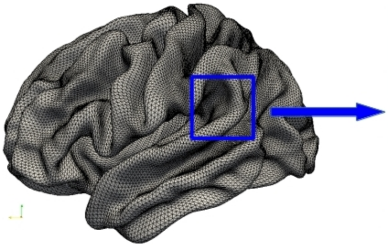
Model

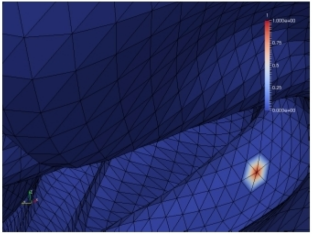
$\hat{\phi}$ first PC function; $\hat{\boldsymbol{\eta}}$ n-dimensional score vector

$$(\hat{\boldsymbol{\eta}}, \hat{\phi}) = \underset{\boldsymbol{\eta},\phi}{\operatorname{argmin}} \sum_{i=1}^{n} \sum_{j=1}^{s} (y_i(p_j) - \eta_i \phi(p_j))^2 + \lambda \boldsymbol{\eta}^T \boldsymbol{\eta} \int_{\mathcal{M}} \Delta_{\mathcal{M}}^2 \phi(p) dp$$

- y_i, $i = 1, \ldots, n$ in the model only through its evaluations on $p_1, \ldots, p_s \in \mathcal{M}$
- Empirical Term: $\sum_{i=1}^{n} \sum_{j=1}^{s} (y_i(p_j) - \eta_i \phi(p_j))^2$
- Regularization Term: $\int_{\mathcal{M}} \Delta_{\mathcal{M}}^2 \phi(p) dp$: Laplace-Beltrami operator on the manifold $\mathcal{M}$

Surface Finite Element





- $\mathcal{M}_\mathcal{T} = \cup_{T \in \mathcal{T}_h} T$, with $\mathcal{T}_h$ set of triangles
- Surface Finite Element space (Dziuk 1988)

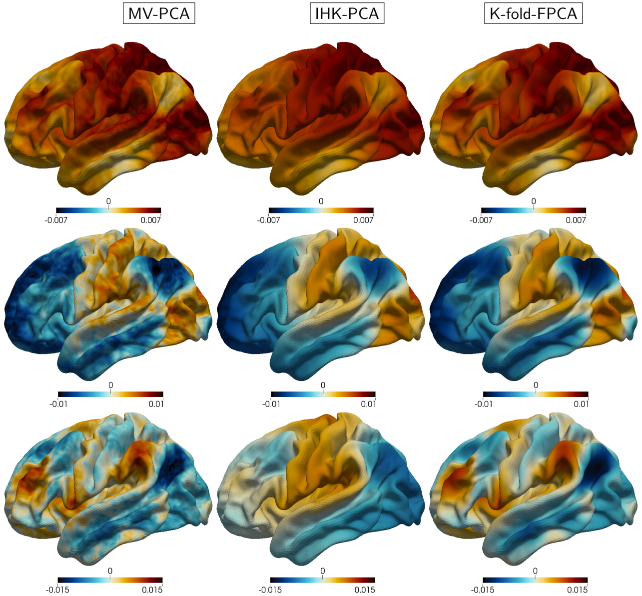
$$V_h = \{v \in C^0(\mathcal{M}_\mathcal{T}) : v|_\tau \text{ is linear affine for each } \tau \in \mathcal{T}_h\}$$

- Lagrangian basis $\psi_1, \ldots, \psi_K$ associated to the K mesh nodes $\xi_1, \ldots, \xi_K$
- Every function $\phi \in V_h$ has the form

$$\phi(p) = \sum_{k=1}^{K} \phi(\xi_k)\psi_k(p) = \boldsymbol{\phi}^T \boldsymbol{\psi}(p)$$

for each $p_i \in \mathcal{M}_\mathcal{T}$, with $\boldsymbol{\phi} = (\phi(\xi_1), \ldots, \phi(\xi_K))^T$ and $\boldsymbol{\psi} = (\psi_1, \ldots, \psi_K)^T$.

Smooth-Manifold FPCA



Outline

Functional Time Series and Change Point Detection

We are interested in detecting mean changes in functional observations

$$X_i(t), t \in \mathcal{T}, i = 1, \ldots, n,$$

where $\mathcal{T}$ is some compact set.

- Berkes et al. (2009) and Aue et al. (2009) - at most one change-point (AMOC) and independent (functional) observations
- Hörmann and Kokoszka (2009) - AMOC and specific weak dependent processes.

Epidemic Change Model

The epidemic model is given by

$$X_i(u) = Y_i(u) + \mu_1(u) + (\mu_2(u) - \mu_1(u))1_{\{\vartheta_1 n < i \leqslant \vartheta_2 n\}}, \tag{2}$$

where $\boldsymbol{\mu}_j$ and $\{Y_i(\cdot) : 1 \leqslant i \leqslant n\}$ are as above, $0 < \vartheta_1 \leqslant 1$ marks the beginning of the epidemic change, while $\vartheta_1 \leqslant \vartheta_2 \leqslant 1$ marks the end of the epidemic change. $\boldsymbol{\mu}_1$, $\boldsymbol{\mu}_2$ as well as ϑ_1, ϑ_2 are unknown.

Implications for Functional Connectivity

Covariance Characterisation under Alternative

The link between activations and functional connectivity:

$$s_A(u,v) = s(u,v) + \theta(1-\theta)\Delta(u)\Delta(v),$$

where

$$\Delta(u) = \mu_1(u) - \mu_2(u),$$
$$\theta = \vartheta_2 - \vartheta_1, \qquad \text{epidemic change.}$$

Testing Framework

We are interested in testing the null hypothesis of no change in the mean

$$H_0 : \mathrm{E}\, X_i(\cdot) = \mu_1(\cdot), \quad i = 1, \ldots, n,$$

versus the epidemic change alternative

$$\begin{aligned} H_1 : & \mathrm{E}\, X_i(\cdot) = \mu_1(\cdot), \quad i = 1, \ldots, \lfloor \vartheta_1 n \rfloor, \lfloor \vartheta_2 n \rfloor + 1, \ldots, n, \quad \text{but} \\ & \mathrm{E}\, X_i(\cdot) = \mu_2(\cdot) \neq \mu_1(\cdot), \quad i = \lfloor n\vartheta_1 \rfloor + 1, \ldots, \lfloor \vartheta_2 n \rfloor, \quad 0 < \vartheta_1 < \vartheta_2 < 1. \end{aligned}$$

Note that the null hypothesis corresponds to the cases where $\vartheta_1 = \vartheta_2 = 1$.

Functional Time Series Assumptions

- The process $\boldsymbol{\eta}_i = (\eta_{i,1}, \ldots, \eta_{i,d})^T$ fulfills the following functional limit theorem

$$\left\{ \frac{1}{\sqrt{n}} \sum_{1 \leqslant i \leqslant nx} \boldsymbol{\eta}_i \; : \; 0 \leqslant x \leqslant 1 \right\} \xrightarrow{D^d[0,1]} \{ \boldsymbol{\Delta}_d(x) : 0 \leqslant x \leqslant 1 \},$$

  where $\boldsymbol{\Delta}_d$ is a d-dimensional Wiener process with covariance matrix $\boldsymbol{\Sigma} = \sum_{k \in \mathbb{Z}} \Gamma(k)$, $\Gamma(h) = \mathrm{E}\, \boldsymbol{\eta}_i \boldsymbol{\eta}_{i+h}^T$, $h \geqslant 0$, and $\Gamma(h) = \Gamma(-h)^T$ for $h < 0$.

Test statistic

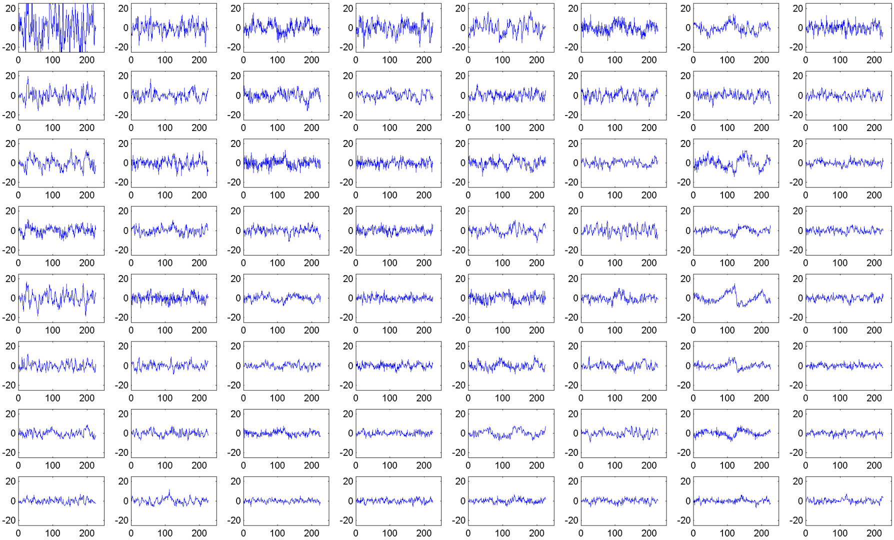
The following then defines a test statistic for an epidemic change in mean
Under H_0 it holds:

$$T_n := \frac{1}{n^3} \sum_{1 \leqslant k_1 < k_2 \leqslant n} \mathbf{S}_n \left(k_1/n, k_2/n \right)^T \widehat{\boldsymbol{\Sigma}}^{-1} \mathbf{S}_n \left(k_1/n, k_2/n \right)$$
$$\xrightarrow{\mathcal{L}} \sum_{1 \leqslant l \leqslant d} \int \int_{0 \leqslant x < y \leqslant 1} \left(B_l(x) - B_l(y) \right)^2 dx\, dy$$

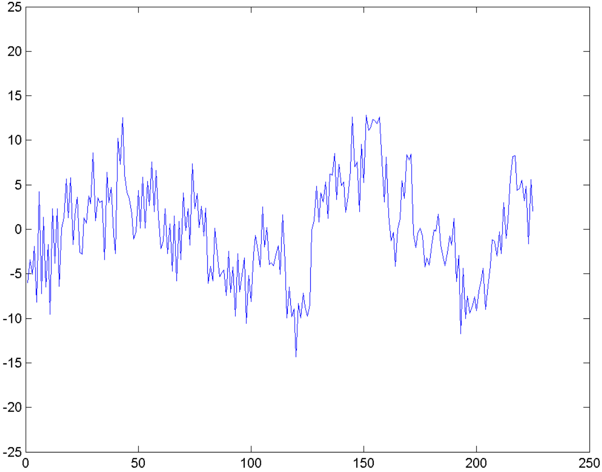
where $\widehat{\boldsymbol{\Sigma}}$ is a consistent estimator for the long-run covariance matrix and

$$\mathbf{S}_n(x,y) = \sum_{nx < j \leqslant ny} \left(\widehat{\boldsymbol{\eta}}_j - \frac{1}{n} \sum_{t=1}^{n} \widehat{\boldsymbol{\eta}}_t \right).$$

Component Time Series



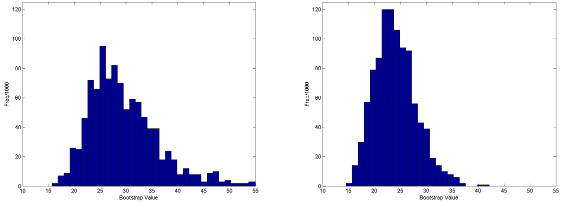
Single Component Time Series



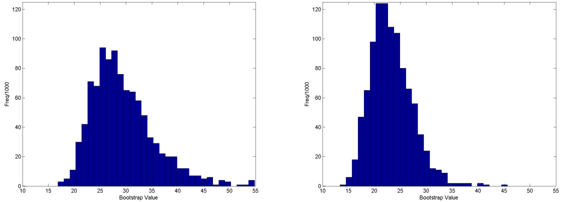
Data Analysis

- Analysis performed on 197 subjects (1 corrupted) - approximately 1.5Gb of Data.
- 75 subjects (after FDR correction and bootstrap test) found to have epidemic change point which yielded change point time distribution estimate

Bootstrap Distributions

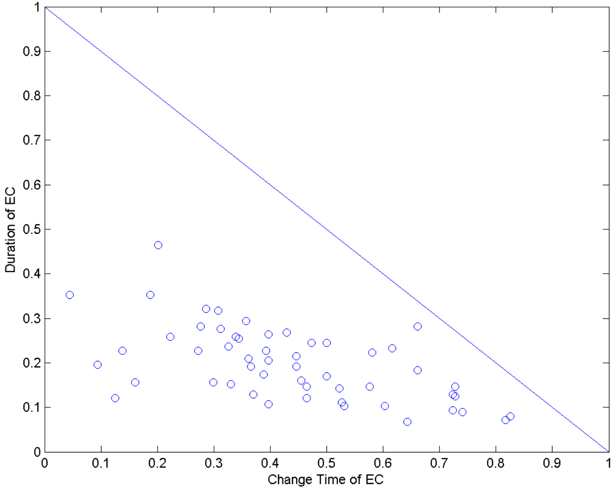


Bootstrap distribution (change detected)

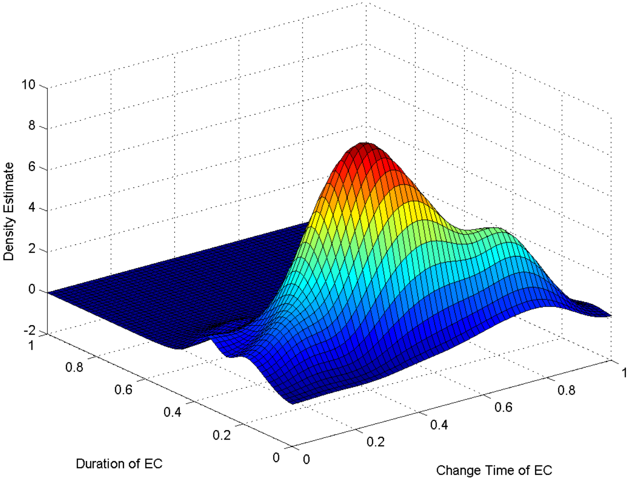


Bootstrap distribution (no change detected)

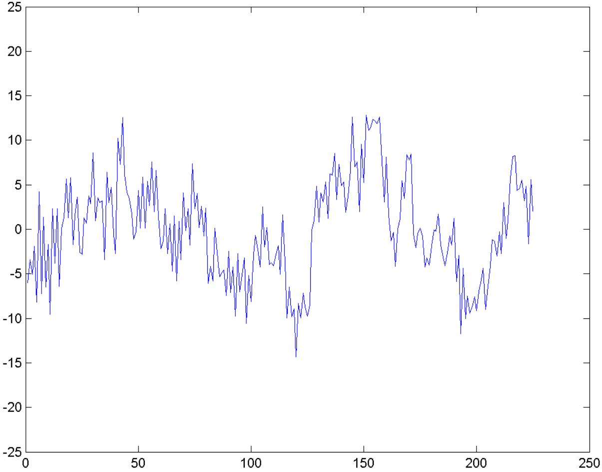
Change Point Locations



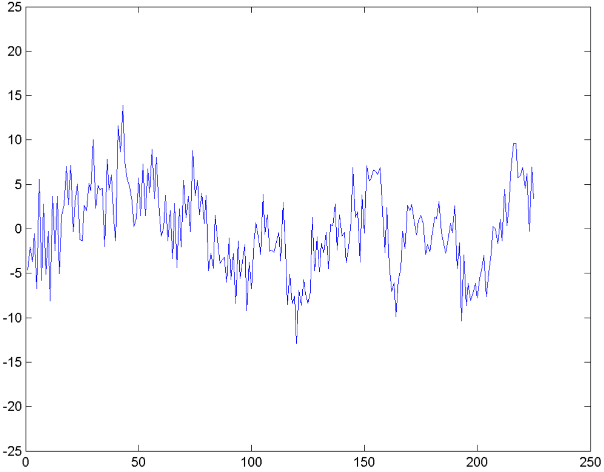
Change Point Locations



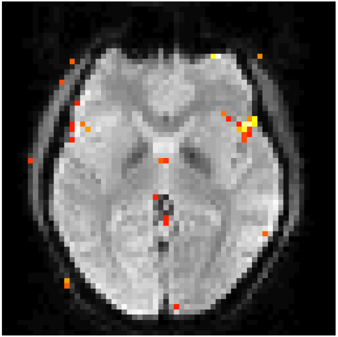
Single Component Time Series



Single Component Time Series



Activation?



Subject 01018: Map of $\Delta(t)$ for a plane in the middle of the brain. As can be seen, there is some evidence of bilateral activation (here colour indicates an increase in fMRI during the epidemic change), along with some random spatial noise.

Outline

Testing Framework

We are interested in testing the null hypothesis of no change in the covariance

$$H_0 : \mathrm{E}\, Y_i(t) Y_i(u) = s(t,u), \quad i = 1, \ldots, n,$$

versus the epidemic change alternative

$$\begin{aligned} H_1 : &\mathrm{E}\, Y_i(t) Y_i(u) = s(t,u), \quad i = 1, \ldots, \lfloor \vartheta_1 n \rfloor, \lfloor \vartheta_2 n \rfloor + 1, \ldots, n, \quad \text{but} \\ &\mathrm{E}\, Y_i(t) Y_i(s) = \tilde{s}(t,u) \neq s(t,u), \quad i = \lfloor n\vartheta_1 \rfloor + 1, \ldots, \lfloor \vartheta_2 n \rfloor, \quad 0 < \vartheta_1 < \vartheta_2 < 1 \end{aligned}$$

Note that the null hypothesis corresponds to the cases where $\vartheta_1 = \vartheta_2 = 1$.

Testing Framework

Under the alternative it holds

$$
\begin{aligned}
E(\eta_{i,l}\eta_{i,k}) &= \int\int s(t,u)\phi_l(t)\phi_k(u)dtdu \\
&\quad + 1_{(\vartheta_1 n < i < \vartheta_2 n)} \int\int (\tilde{s}(t,u) - s(t,u))\phi_l(t)\phi_k(u)dtdu
\end{aligned}
$$

Therefore, we can check to see whether there is a departure from 0 of the second term.

Test statistic

The following then defines a test statistic for an epidemic change in mean Under H_0 it holds:

$$T_n := \frac{1}{n^3} \sum_{1 \leqslant k_1 < k_2 \leqslant n} \mathbf{S}_n\left(k_1/n, k_2/n\right)^T \widehat{\boldsymbol{\Sigma}}^{-1} \mathbf{S}_n\left(k_1/n, k_2/n\right)$$

$$\xrightarrow{\mathcal{L}} \sum_{1 \leqslant l \leqslant d.(d+1)/2} \int\int_{0 \leqslant x < y \leqslant 1} \left(B_l(x) - B_l(y)\right)^2 dx\, dy$$

where $\widehat{\boldsymbol{\Sigma}}$ is a consistent estimator for the long-run covariance matrix and

$$\mathbf{S}_k(x,y) = \sum_{nx < j \leqslant ny} \left(\text{vech}(\widehat{\boldsymbol{\eta}}_j \boldsymbol{\eta}_j^T - k\text{diag}(\hat{\lambda}_1, \ldots, \hat{\lambda}_k))\right).$$

Simulations

Preliminary Results - AMOC change

α	0,10			0,05			0,01		
n	100	200	500	100	200	500	100	200	500
δ									
0,20	0,133	0,154	0,203	0,077	0,087	0,137	0,015	0,027	0,056
0,30	0,504	0,712	0,966	0,417	0,624	0,952	0,204	0,426	0,904
0,35	0,774	0,948	1,000	0,728	0,927	1,000	0,504	0,841	1,000
0,40	0,935	0,995	1,000	0,912	0,987	1,000	0,779	0,971	1,000
0,50	0,996	1,000	1,000	0,992	1,000	1,000	0,980	1,000	1,000

where $\delta = |\tilde{s}(t,u) - s(t,u)|$.

Summary

- Functional Principal Components are a useful concept in brain imaging.
- Can be defined on the volume or on the surface
- Can be used to detect general mean shifts in image data
- Can potentially be used to look for connectivity changes

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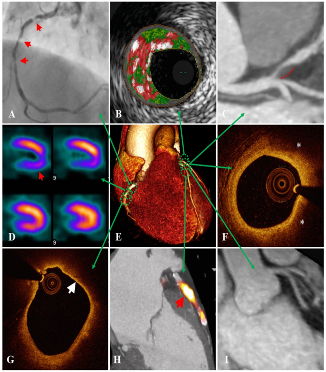

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