RADIOMIC AND MACHINE LEARNING APPROACHES TO DETECT PANCREATIC CANCER IN PATIENTS PRESENTING WITH ACUTE PANCREATITIS

(MAGIC-SCAN STUDY)

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Dear Colleagues,

The Hungarian Pancreas Study Group continues its international investigations and invites all researchers to participate in the following study.

Title: "Radiomic and machine learning approaches to detect pancreatic cancer in patients presenting with acute pancreatitis"

Background: Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer deaths, with a 5-year survival <5%. Patients with pancreatic cancer may present with acute pancreatitis 6 months to 3 years prior to diagnosis, which offers an opportunity for early detection. Moreover, patients with clinical suspicion of acute pancreatitis typically undergo CT with intravenous contrast, however, characteristic radiologic signs of PDAC may not be identified, and therefore the diagnosis can be missed or delayed.

Currently, Hungary has the highest rate of pancreatic cancer in the world. The Hungarian Pancreas Study Group has been following patients with acute pancreatitis since 2011. This prospective longitudinal database was established to understand the long-term sequelae of acute pancreatitis. In our database, 3178 patients were followed, and the risk of developing pancreatic cancer (PC) was 2.2% (70 patients).

Radiomics offers an opportunity to identify novel markers, such as pancreatic image texture and/or abdominal tissue composition analysis, that may be used as predictive markers. Machine learning models, incorporating multi-modal biomarkers, can further enhance the accuracy of these prediction tools.

Early detection of pancreatic cancer offers a significant opportunity that likely impacts survival. Although efforts have focused on using imaging as an early biomarker, none have focused on acute pancreatitis. Parenchymal changes associated with acute pancreatitis create specific challenges for radiomics and we believe this study will be the first to specifically address and evaluate these.

Aim: The goal of this study is to define imaging characteristics of neoplasms associated with AP and develop models to identify patients at risk of PDAC with AP.

Hypothesis and aims: We hypothesize that radiomic features can be used to identify underlying neoplasm in the setting of acute pancreatitis and that using machine learning tools applied to a large dataset we can detect these patients with high accuracy.

Aim 1. Quantify image-based changes in pancreatic morphometry, pancreatic texture, and body composition in patients with acute pancreatitis.

Aim 2. (a) Develop novel machine learning algorithms to identify signs of underlying PDAC in patients presenting with acute pancreatitis. (b) Develop a multi-modal model that combines imaging data with epidemiological and clinical data to improve predictive performance.

Methods:

a) Study design
This study will be an ambidirectional observational study based on data collected from participating centres worldwide.

b) Study population

The study population will consist of patients diagnosed with acute pancreatitis prior to the diagnosis of PC.

Inclusion criteria are as follows: (1) patients with a confirmed (cytological or histological) diagnosis of PDAC (the day of the tissue acquisition will be considered as the date of the diagnosis). (2) Past medical history of acute pancreatitis based on the 'two out of three' rules of IAP/APA guideline: (a) upper abdominal pain, (b) serum amylase or lipase levels at least three times the upper limit of normal (c) characteristic findings on pancreatic imaging. (3) At least 6 months passed between the first episode of acute pancreatitis and the diagnosis of PDAC. (4) Minimum 1 CT scan about (preferably the first) AP episode is available and can be retrieved.

c) Data collection

Data will be collected using an Excel datasheet. Participating centres will enter de-identified patient data. The data table will include the following data:

- Demographic information (sex, birthdate).
- PDAC-related information (diagnostic method, date of diagnosis).
- Details of the previous acute pancreatitis episodes.
- Hospital admission and discharge dates of acute pancreatitis episodes.
- Dates of all CT scans from the first acute pancreatitis episode to the PDAC diagnosis.

After demographic data is provided, a personalized platform will be sent out to each centre to upload the de-identified contrast-enhanced CT scans in DICOM format. If multiple CT scans are available from the first AP episode to the PDAC diagnosis, all should be uploaded to the platform including the CT about the PDAC formation.

d) Model development

We use a validated image analysis pipeline developed at NYULH (Firevoxel) to quantify image-based changes and develop a model that identifies those patients with acute pancreatitis who are at risk of developing cancer. To prevent data leakage and ensure unbiased evaluation, we will split patients into mutually exclusive training (80%) and test (20%) sets, so each patient's data will only be present in either the training or test set. To address the high dimensionality of the 478 radiomic features, which increases overfitting risk, we will use LASSO logistic regression for feature selection.

Ethical considerations:

The National Center For Public Health approved the study under number 17787-8/2020/EÜIG. Patient data will be entered anonymously into the datasheets.

Publication Policy:

Based on the number of patients included, co-authorship will be granted to the participating centers and their representatives. The following guidelines will apply: <= 3 patients: 1 author, 3-6: 2 authors, and above 6 patients = 3 authors. All co-authors will be acknowledged in the manuscript.

Project closure:

The expected completion date of the Magic-Scan study is the 31st of July, 2024.

Conclusion:

In summary, this significant collaboration will use novel radiomic and image analysis tools as well as multi-modal data to detect underlying neoplasms in acute pancreatitis settings. Although acute pancreatitis is a somewhat uncommon presentation of PDAC, the availability of imaging in these patients offers an essential opportunity for early detection. We expect that early detection, with a 6-24-month lead time, may significantly impact the survival of patients with PDAC.

MAGIC-SCAN STUDY'S QUESTIONNAIRE

General information	
1	Please enter the number of patients you will send data about in a consecutive order.
2	Please provide data about the centre of the data source (country_city_hospital).
3	Please give the patient a unique patient ID (country_city_hospital_birthyear of the patient_year of PC diagnosis).
4	Please mention the patient's sex (1: male, 2: female).
5	Please mention the patient's birthdate (yyyy.mm.dd).
PDAC-related information	
6	Please specify the location of the tumor (1: head, 2: body, 3: tail, 4: unknown, 5: other, please specify)
7	Please provide the date of pancreatic cancer diagnosis (when the pathology sample was taken) (yyyy.mm.dd).
8	Please mention the clinical stage of the disease (1: resectable, 2: borderline resectable, 3:unresectable, locally advanced, 4: unresectable, metastatic)
Please provide information about the previous AP episodes here	
9	Wich acute pancreatitis (AP) episode was the first documented (not just mentioned in the past medical history, but proved with previous documents) episode that the patient had? (e.g. 1 or 2 or 3….)
10	What was the etiology of the first documented AP episode (biliary, alcohol, hypertrigliceridemia, other, idiopathic, post-ERCP, drug-induced, no data)?
11	What was the severity of the first documented AP episode (according to the modified Atlanta classification: mild, moderate, severe)?
12	After the first documented AP episode, was the patient diagnosed with another episode of AP (recurrent acute pancreatitis - RAP) (1: yes, 2: no, 3: no data)?
13	How many AP episodes (documented + not documented) did the patient have before the PDAC diagnosis (including the first episode as well)?
14	Did chronic pancreatitis develop before the PC diagnosis (1: yes, 2: no, 3: no data)?
15	Was autoimmune pancreatitis diagnosed before the first documented AP episode (1: yes, 2: no, 3: no data)?
16	Was diabetes mellitus diagnosed before the first documented AP episode (1: yes, 2: no, 3: no data)?
17	Was diabetes mellitus diagnosed after the first documented AP episode (1: yes, 2: no, 3: no data)?

Please list all dates in consecutive order of when the patient was admitted to the hospital because of AP (only the documented episodes should be listed here).	
18	First AP episode - First day of hospitalization (yyyy.mm.dd).
19	First AP episode - Last day of hospitalization (yyyy.mm.dd).
20	Second AP episode - First day of hospitalization (yyyy.mm.dd).
21	Second AP episode - Last day of hospitalization (yyyy.mm.dd).
22	Third AP episode - Last day of hospitalization (yyyy.mm.dd).
23	Third AP episode - Last day of hospitalization (yyyy.mm.dd).
24	Fourth AP episode - First day of hospitalization (yyyy.mm.dd).
25	Fourth AP episode - Last day of hospitalization (yyyy.mm.dd).
26	Fifth AP episode - First day of hospitalization (yyyy.mm.dd).
27	Fifth AP episode - Last day of hospitalization (yyyy.mm.dd).
28	Sixth AP episode - First day of hospitalization (yyyy.mm.dd).
29	Sixth AP episode - Last day of hospitalization (yyyy.mm.dd).
30	Second AP episode - First day of hospitalization (yyyy.mm.dd).
31	Second AP episode - Last day of hospitalization (yyyy.mm.dd).
Please list here all dates in consecutive order when an abdominal CT scan was taken from the patient from the first AP episode to the diagnosis of PC.	
32	1. available CT date (yyyy.mm.dd).
33	1. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
34	2. available CT date (yyyy.mm.dd).
35	2. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
36	3. available CT date (yyyy.mm.dd).
37	3. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
38	4. available CT date (yyyy.mm.dd).

39	4. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
40	5. available CT date (yyyy.mm.dd).
41	5. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
42	6. available CT date (yyyy.mm.dd).
43	6. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
44	7. available CT date (yyyy.mm.dd).
45	7. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
46	8. available CT date (yyyy.mm.dd).
47	8. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
48	9. available CT date (yyyy.mm.dd).
49	9. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
50	10. available CT date (yyyy.mm.dd).
51	10. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
52	11. available CT date (yyyy.mm.dd).
53	11. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
54	12. available CT date (yyyy.mm.dd).
55	12. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)

56	13. available CT date (yyyy.mm.dd).
57	13. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
58	14. available CT date (yyyy.mm.dd).
59	14. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
60	15. available CT date (yyyy.mm.dd).
61	15. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
62	16. available CT date (yyyy.mm.dd).
63	16. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
64	17. available CT date (yyyy.mm.dd).
65	17. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
66	18. available CT date (yyyy.mm.dd).
67	18. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
68	19. available CT date (yyyy.mm.dd).
69	19. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
70	20. available CT date (yyyy.mm.dd).
71	20. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)
72	21. available CT date (yyyy.mm.dd).
73	21. available CT details (type of CT scanner (eg. SIEMENS NAEOTOM Alpha), slice thickness in mm (e.g. 1), phases of acquisition (e.g. non-contrast, arterial (x seconds delay), venous (y seconds delay), type and concentration of the iv. contrast (e.g. Omnipaque 350), injection flow rate (e.g. 4 mL/sec)

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