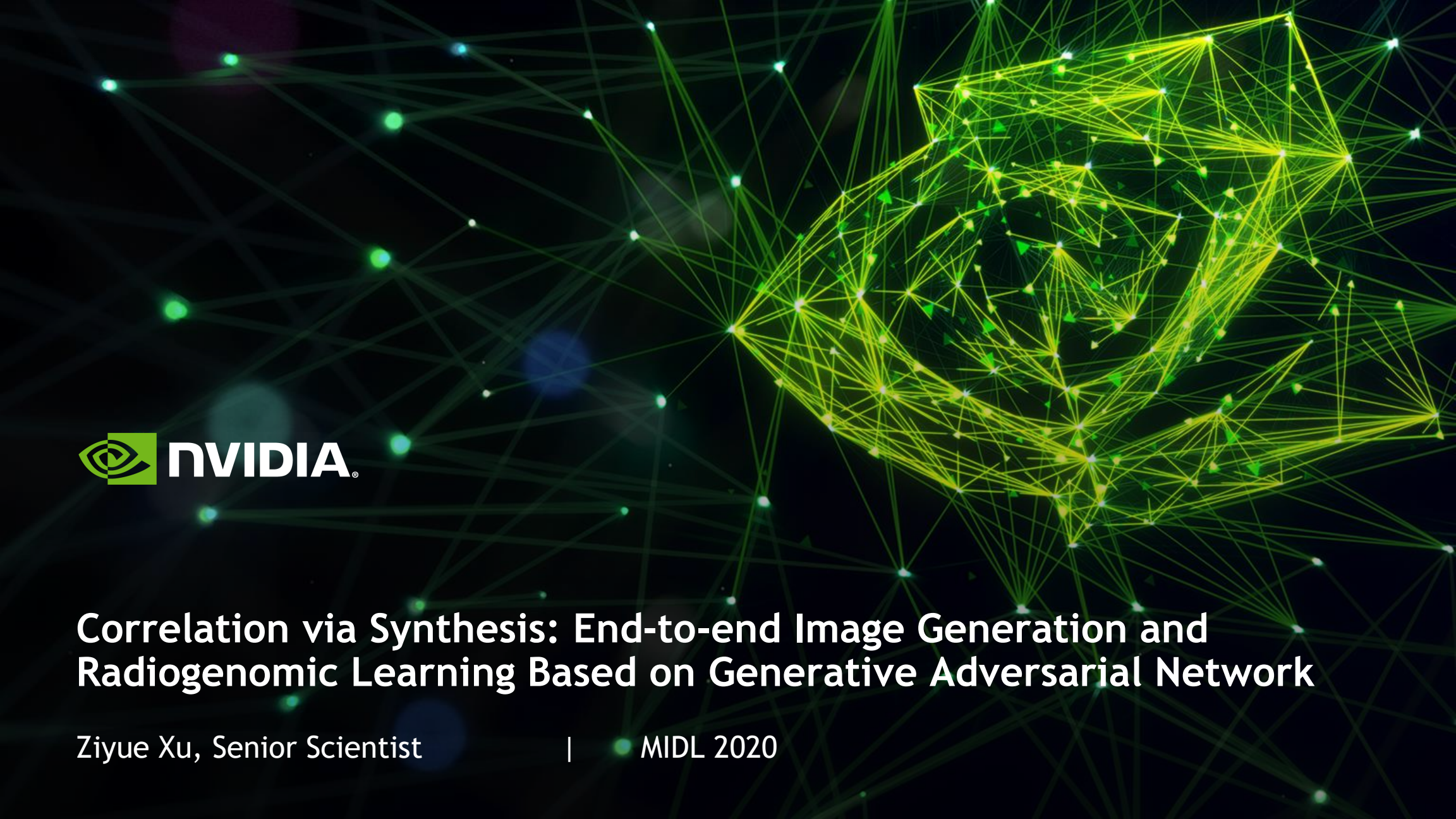

Correlation via Synthesis: End-to-end Image Generation and Radiogenomic Learning Based on Generative Adversarial Network

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PURPOSE, METHOD, & LIMITATION

What to Expect

- Goal: looking for the connection between the imaging characteristics and their associated gene coding
- Method: end-to-end generative adversarial network (GAN) fusing the information

- A challenging, sophisticated, and ongoing research area: no definite conclusion has been made, not fully explored, but potentially impactful for clinical application.
- Our work provides an alternative (may/not be better) way of modelling this open question.
- Preliminary and proof-of-concept work, aiming to bring some inspiration and discussion to the community about what we can do with radiogenomic data using deep learning.

GOAL: RADIOGENOMIC CORRELATION

FROM CODE TO APPEARANCE

If We Understand the “Code”

Code - English

Woman with a Parasol - Madame Monet and Her Son,

A lady wearing white, holding a green parasol, standing on grass and wild flowers, with her son. -- content

“bright sunlight shines from behind to whiten the top of her parasol and the flowing cloth at her back, while colored reflections from the wildflowers below touch her front with yellow” -- detail

“a repertory of animated brushstrokes of vibrant color, hallmarks of the style Monet was instrumental in forming” -- painting style

NGA Open Access: images.nga.gov

FROM CODE TO APPEARANCE

If We do not Understand the “Code”

Code - Klingons

ghaH Parasol-madame monet 'ej puqloD, be'

jaw chIS, tuQ 'uch SuD parasol, Qam grass qu'bogh flowers, puqloD je. -'a ghIH

"tlhop SuD Hot wov sunlight boch vo' 'em, petaQ yor parasol flow cloth DeSDu' Dub, poStaHvIS color reflections vo' wildflowers below 'ej whiten"

"repertory animate brushstrokes vaQchoH color, monet style hallmarks instrumental qaStaHvIS Dumerbe'"

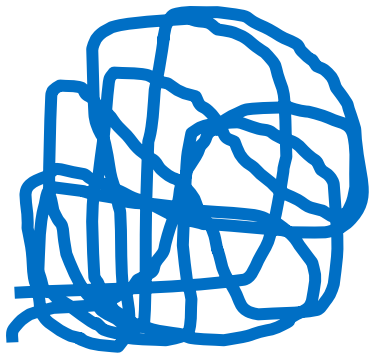
nga mInDu'llj naw': images.nga.gov

FROM CODE TO APPEARANCE

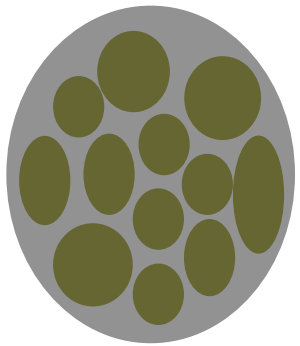
Indirect Radiogenomic Relationship

DNA

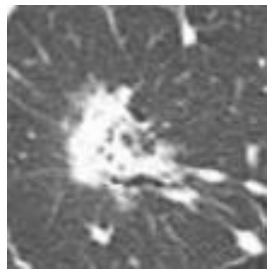
RNA
|
Sequencing

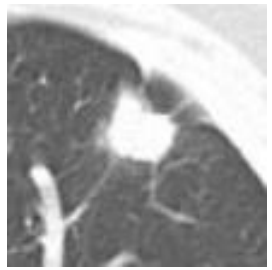


Protein



Nodule





Imaging
|
CT

Calcification
Internal Structure
Lobulation
Margin
Sphericity
Spiculation
Subtlety
Texture
Size
Malignancy

Character
|
Semantic

EXISTING STUDY

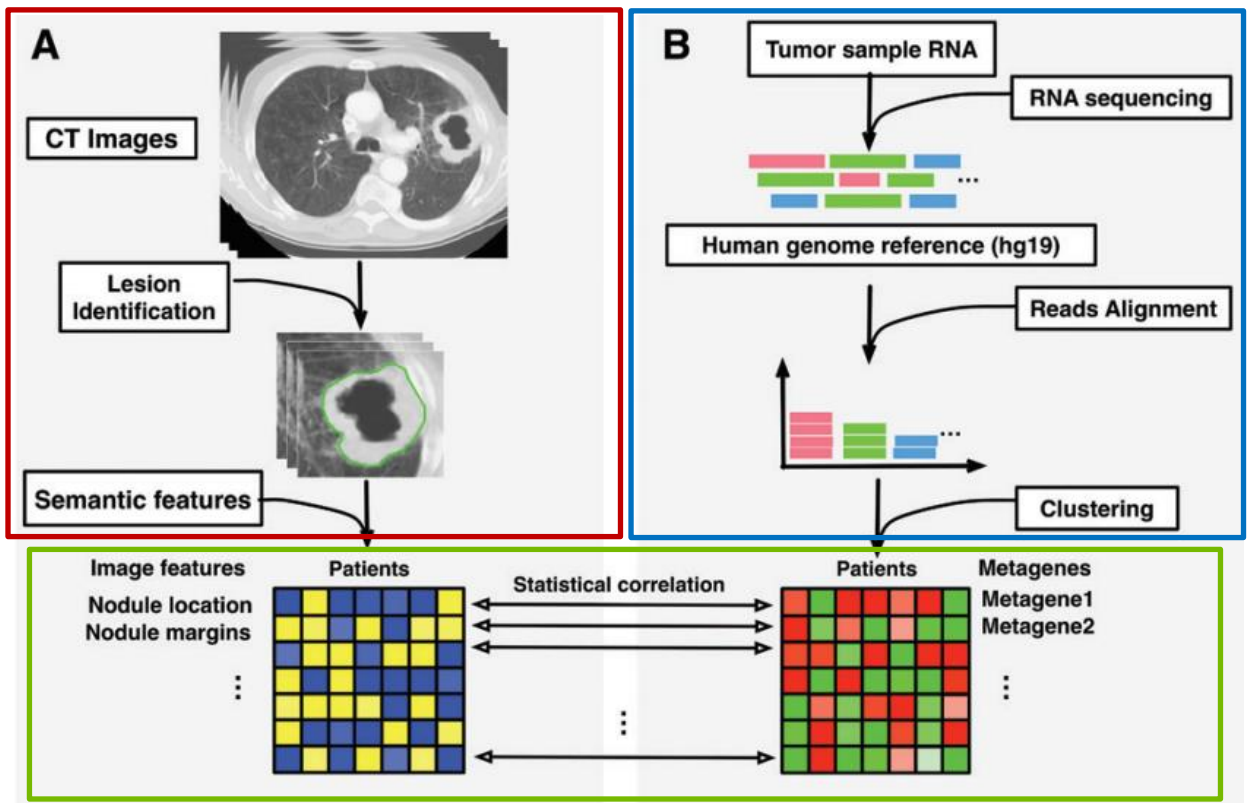
Three Independent Steps

CT image feature extraction: “87 semantic features defined by using a controlled vocabulary and that reflected radiologic characteristics of lung nodules”

Genome clustering to “metagenes”

Statistical correlation

Correlation only, no fusion for representation learning



Zhou M, et al. Non-Small Cell Lung Cancer Radiogenomics Map Identifies Relationships between Molecular and Imaging Phenotypes with Prognostic Implications. Radiology. 2018

WHY HOLISTIC

What may Potentially Go Wrong

Independent 3-step approach:

Image features:

- Hand-crafted sets: may not be a good representation
- Manually defined semantic scores: inter- & intra-observer variabilities

Genomic features:

- Metagene clustering depends on the specific model being used, may not be suitable for a specific task

Image and gene information “blind” to each other during the modelling -> weak correlation

How about holistic and end-to-end?

METHOD: END TO END GENERATION

HOW HOLISTIC

What Needs to be Addressed

How to “inject” the non-image genomic information so that it can be correlated with the image in a pairwise fashion within a single system

How to model the image so that the feature representation is meaningful to its corresponding genomic information

How to split the nodule from background: region beyond the lesion may be irrelevant to the disease; however, the “interaction region” can also hold significant value in lesion characterization, and therefore directly applying a binary segmentation may not be an optimal solution.

PROPOSED METHOD

Holistic Information Fusion via GAN

Image synthesis as a “bridge” to connect image data with genomic representation

A multi-conditional GAN utilizing both gene code and background to synthesize paired nodule image + mask

Image features and gene embeddings learnt from data in an end-to-end manner

Smooth object/background fusion so that unrelated image information gets suppressed for radiogenomic correlation

We applied our strategy to a public NSCLC dataset, it is known that both imaging and gene expression play important role in its management.

PROPOSED METHOD

Multi-input Multi-output Generator

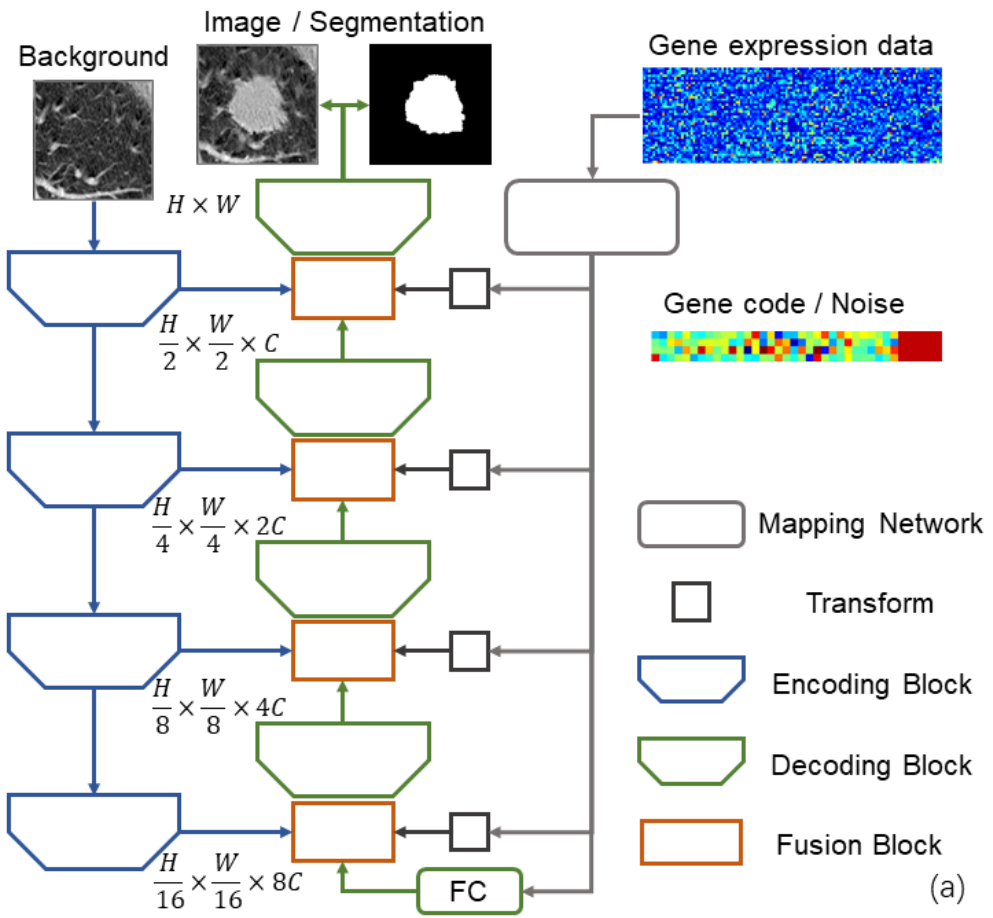
Inputs:
background image, gene expression data, masks

Outputs:
synthetic image, mask prediction

Image coded during encoding path

Fusion block controls the separation

Multi-level style control from gene code



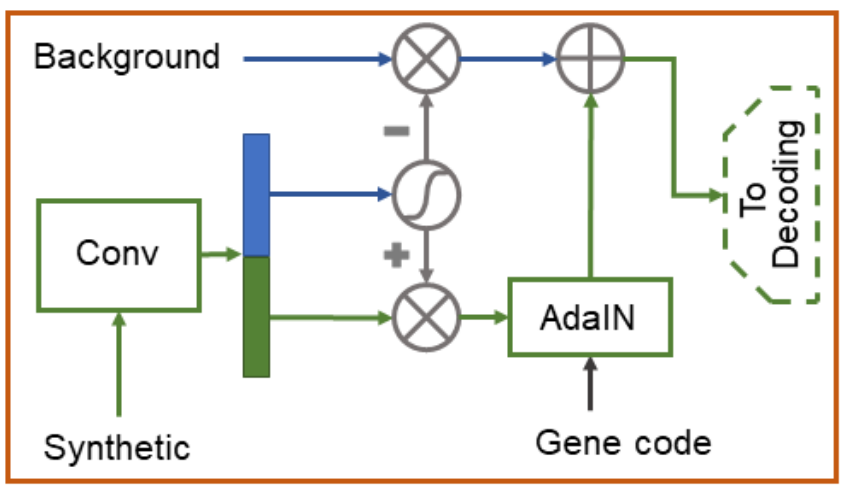
PROPOSED METHOD

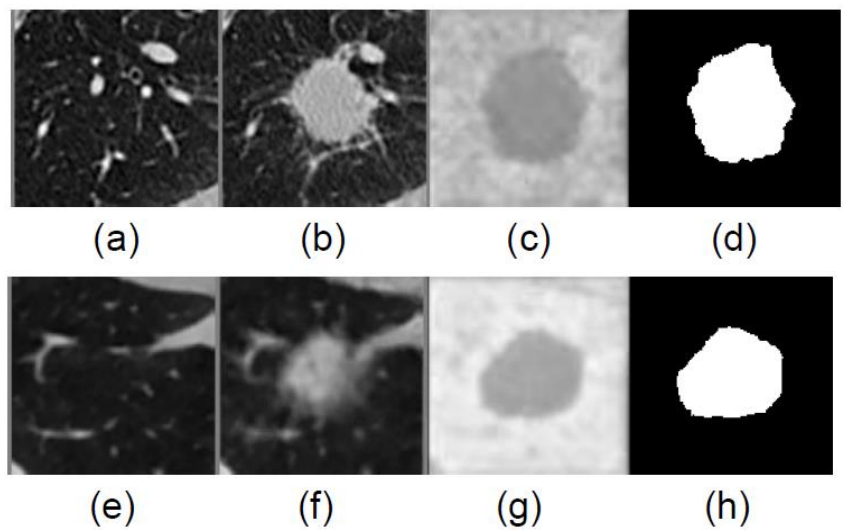
Fusion Block

Attention mechanism controlling the fusion of object and background

Object's appearance further reinforced by gene code via AdaIN at each level

A "soft" separation ensuring smooth transition and information control





PROPOSED METHOD

Discriminator

Input to the discriminator: a tuple of image-segmentation-gene code.

Image x, matched gene code g, matched segmentation mask m, mismatched gene code $\bar{g}$, mismatched segmentation mask $\bar{m}$, synthetic image G_x, and synthetic mask G_m.

The discriminator need to tell if:

1) image is real or synthesized

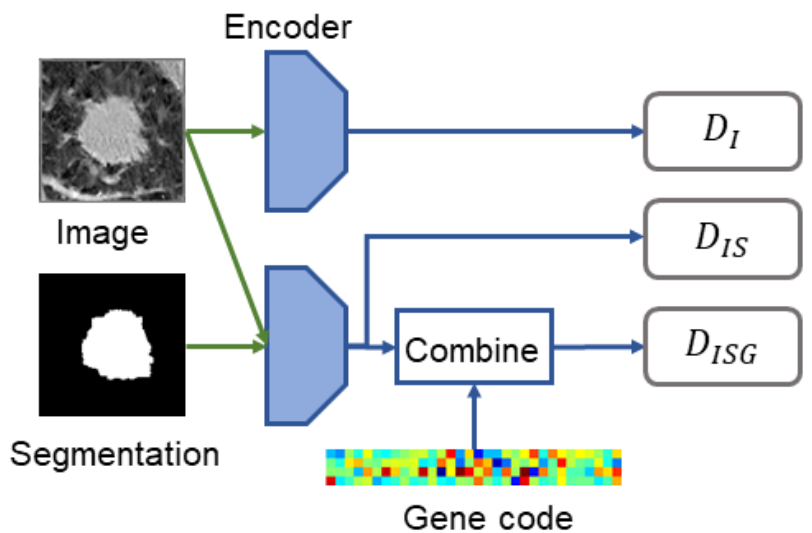
$$L_{D_I} = \mathbb{E}[(D_I(x) - 1)^2] + \mathbb{E}[D_I(G_x)^2]$$

2) image-segmentation pairs match or not

$$L_{D_{IS}} = \mathbb{E}[(D_{IS}(x, m) - 1)^2] + \mathbb{E}[D_{IS}(x, \bar{m})^2] + \mathbb{E}[D_{IS}(G_x, G_m)^2]$$

3) image-segmentation-gene code match or not

$$L_{D_{ISG}} = \mathbb{E}[(D_{ISG}(x, m, g) - 1)^2] + \mathbb{E}[D_{ISG}(x, \bar{m}, g)^2] + \mathbb{E}[D_{ISG}(x, m, \bar{g})^2] + \mathbb{E}[D_{ISG}(G_x, G_m, g)^2]$$



DATA

NSCLC

130 images, with tumor segmentation and RNA sequencing data from surgically excised tumor tissue samples.

5172-dimensional gene vector for each case after removing all NaN values

VOI of 60x60x60 mm^3 cropped around each nodule

2D slices with nodule presence extracted as training samples, in total 3736 training slices.

Background images, also 60x60x60 mm^3 selected at a random location 5 to 25 mm from the lung mask boundary (excluding tumor region) calculate by distance transform.

RESULTS

Synthesize

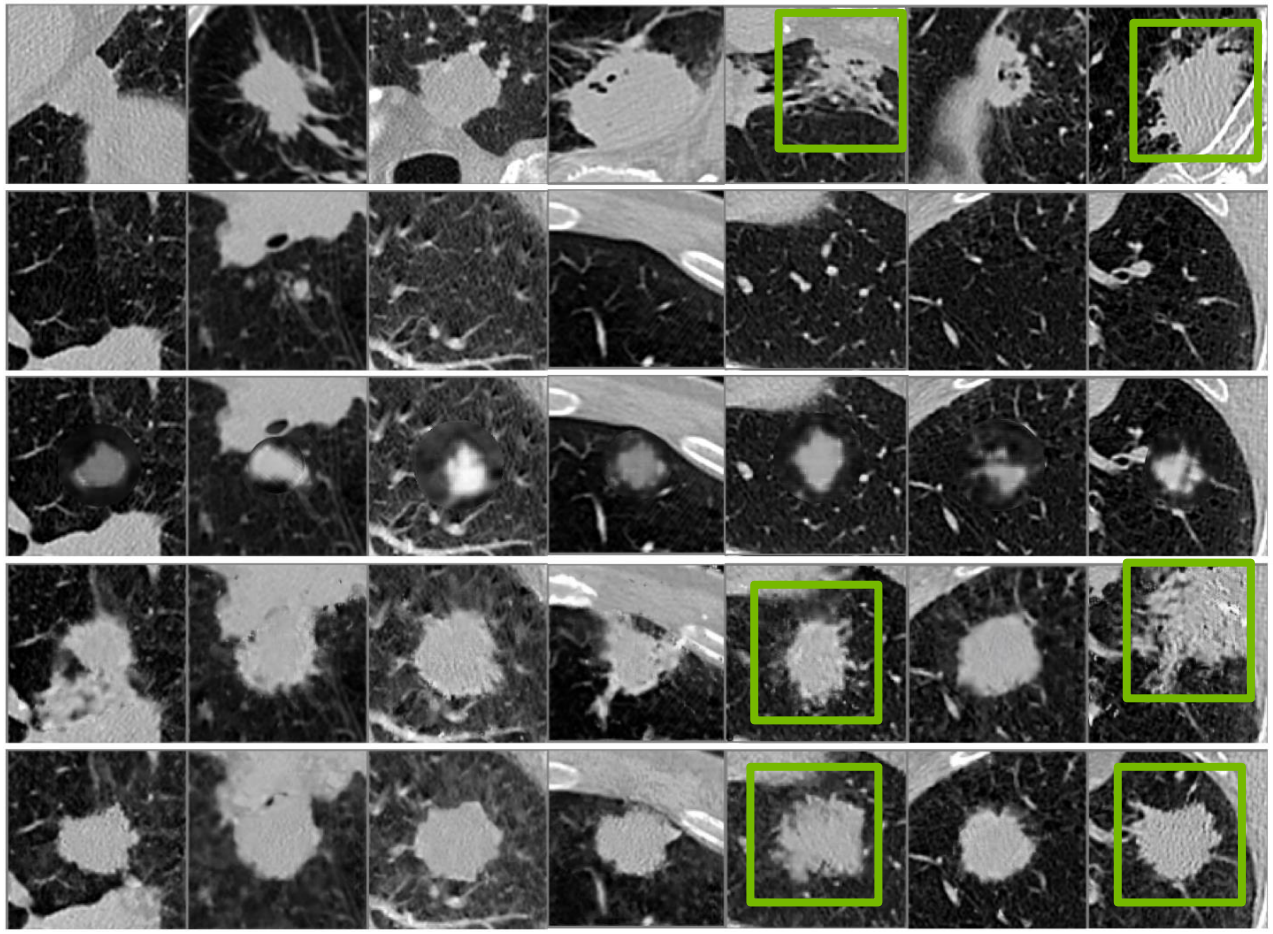
1st row: training image, whose genomic information is used to synthesize each column;

2nd row: background image;

3rd row: synthetic image by our previous in-painting method

4th row: synthetic image by baseline method

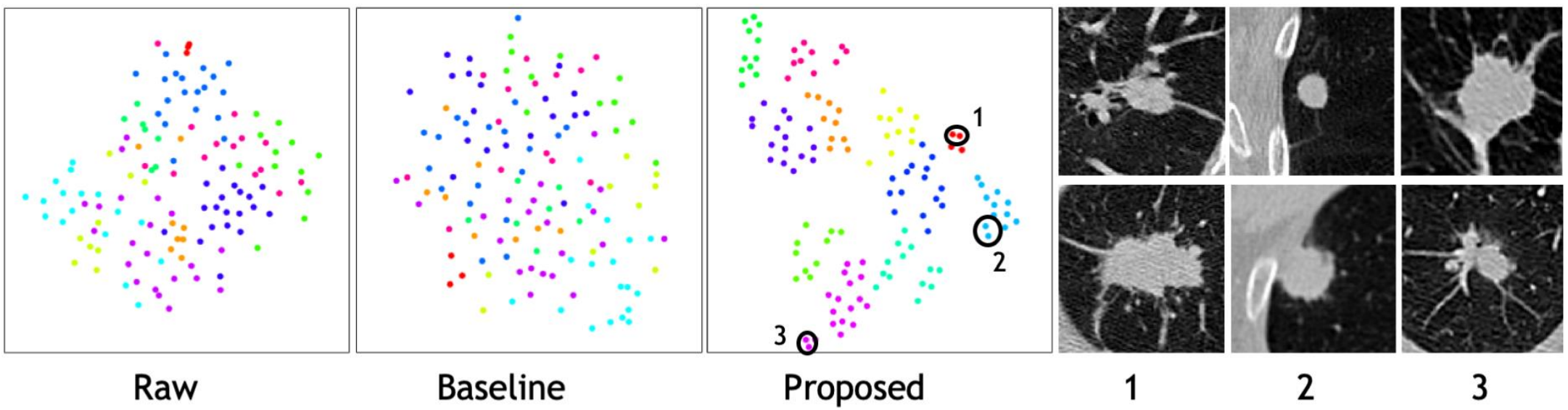
last tow: synthetic image by the proposed method.



RESULTS

Radiogenomic Correlation

Original image with their raw and learnt gene codes. Supposedly, closer gene-codes hints closer appearance. Color is based on the auto-formed clusters by proposed method. The proposed codes can trace back to raw vector, while having better separation.



SUMMARY

New Perspective with Limitations

A multi-conditional GAN, coupled with a new structure of style control and fusion, to effectively generate realistic nodules whose appearance is controlled by its genomic features

Without erasing any portion of condition image, our method is superior over state-of-the-art method in object realism and object/background separation and fusion.

An end-to-end mechanism to holistically model and correlate various features.

Limitations:

Map the learnt gene code back to sequencing vector – “metagene”

Map the image to sematic features – classification network


Thank you!
NVIDIA
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