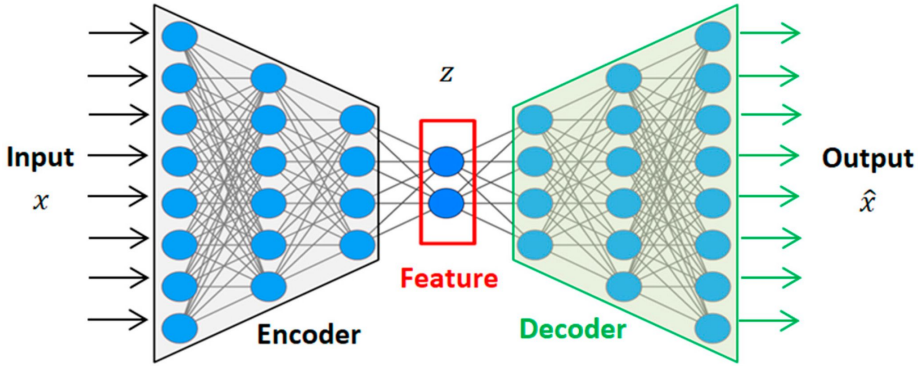
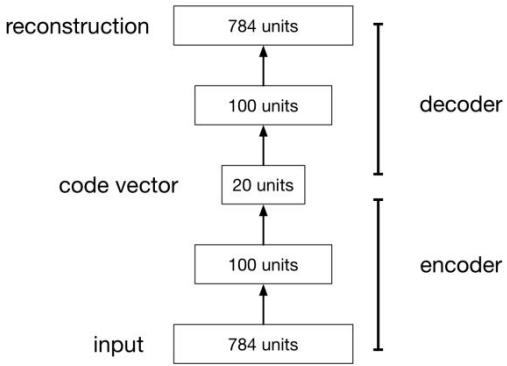
Deep Learning & Generative AI in Healthcare

Session 10

AutoEncoders

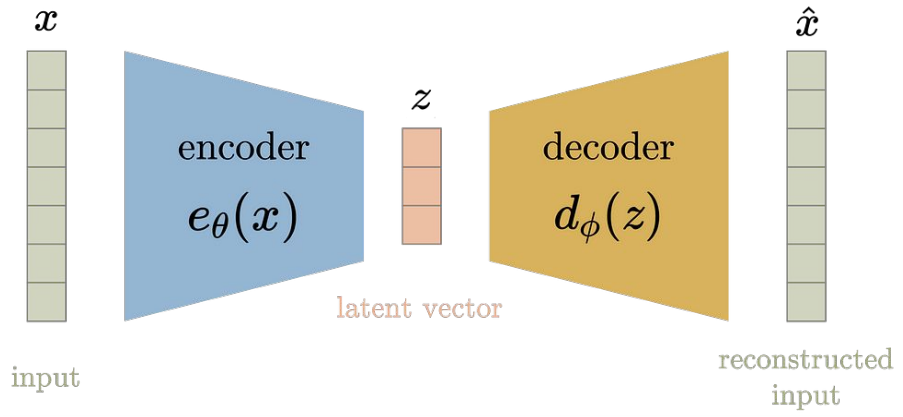
- AE is a feed-forward neural network than given input x learns to reconstruct x.
- There is a bottleneck layer whose dimensions are much smaller than the input dimensions.
- We are reducing 784 input dimensions to only 20 dimensions.
  - We are compressing, keeping only important features.
  - We are trying to reproduce X given using the extracted features.





Encoder-Decoder Architecture

- Encoder
  - Sequence of user-defined layers (e.g. dense, convolutional, pooling)
  - Reduces input dimension from R^m to latent space R^n $(n < m)$
- Latent Space
  - Dimensionality n is a hyperparameter controlling compression level
  - Smaller n ⇒ higher compression but risk of information loss
- Decoder
  - Near-complement of encoder layers (e.g. transposed conv for conv, unpooling for pooling)
  - Mirrors encoder in reverse to rebuild input dimensions



$$loss = \|x - \hat{x}\|_2 = \|x - d_\phi(z)\|_2 = \|x - d_\phi(e_\theta(x))\|_2$$

$$\mathcal{L}(\theta, \phi) = \frac{1}{N} \sum_{i=1}^{N} \| x_i - d_\phi(e_\theta(x_i)) \|^2$$

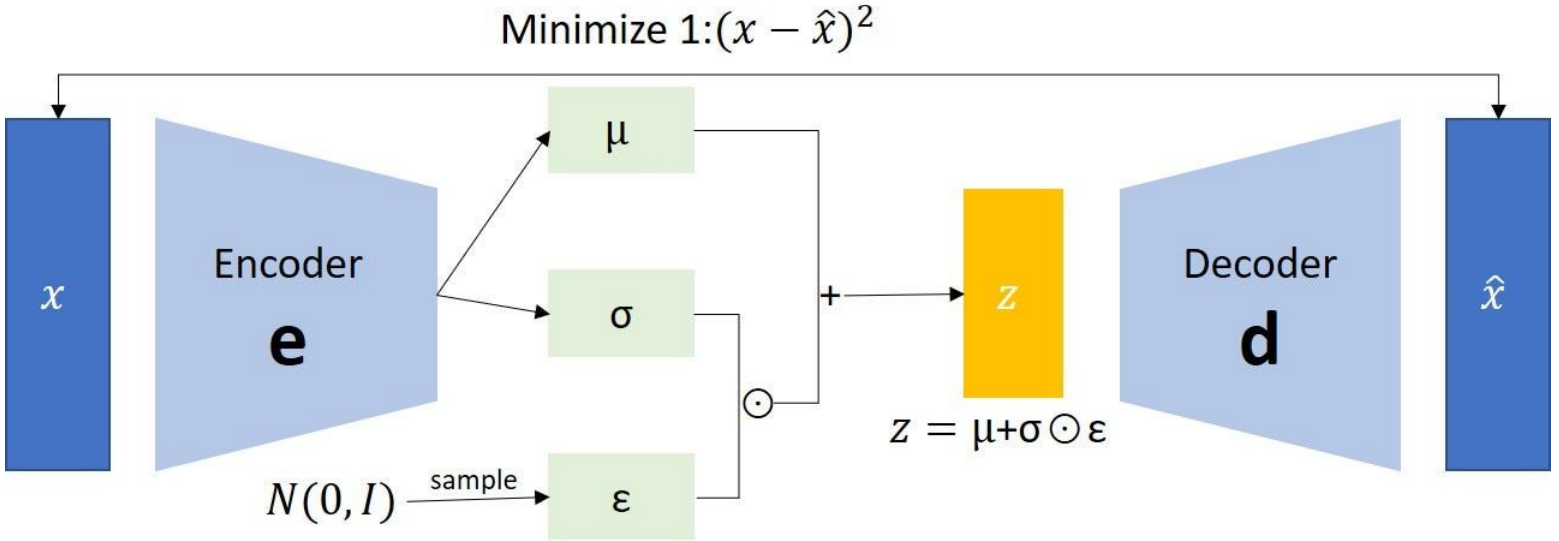
Variational AutoEncoders

- Encoder Network q(Z|X)
  - Maps input X to parameters of a distribution in a latent space
    - Outputs mean \mu and standard deviation \sigma
    - Defines a Gaussian distribution N(\mu, \sigma^2) in latent space
- Latent Space Sampling
  - Sample Z from the distribution using the **reparameterization** trick
- Decoder Network: p(X|Z)
  - Maps latent code Z back to data space to reconstruct X
- VAEs model the joint probability distribution of data and latent variables
  - p(X, Z) = p(X|Z)*p(Z)
  - p(Z) is the prior: Typically N(0, 1)
  - q(Z|X) is the approximate posterior modeled by the encoder
  - p(X|Z) is the likelihood modeled by the decoder

Variational AutoEncoders

- Reconstruction term
  - How can we reconstruct X from Z
  - Implemented as reconstruction loss (e.g., MSE)
- Regularization term
  - How close is our encoding to the prior
  - Keeps latent space regular and smooth
  - KL[q(Z|X) || p(Z)]
- Training algorithm
  - Pass input X through encoder, get \mu and \sigma
  - Sample \epsilon from N(0, 1) and compute Z = \mu + \sigma * \epsilon
  - Pass Z through decoder and compute losses (Reconstruction Loss + KL Divergence)
  - Backpropagate through decoder, backpropagate through reparameterization, and backpropagate through encoder to update the weights

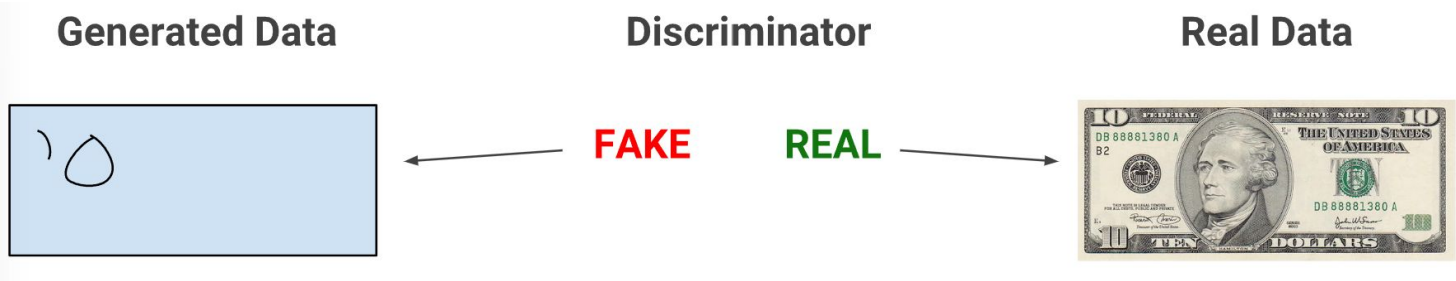
Variational AutoEncoders



Minimize 2: $\frac{1}{2}\sum_{i=1}^{N}(\exp(\sigma_i) - (1+\sigma_i) + \mu_i{}^2)$

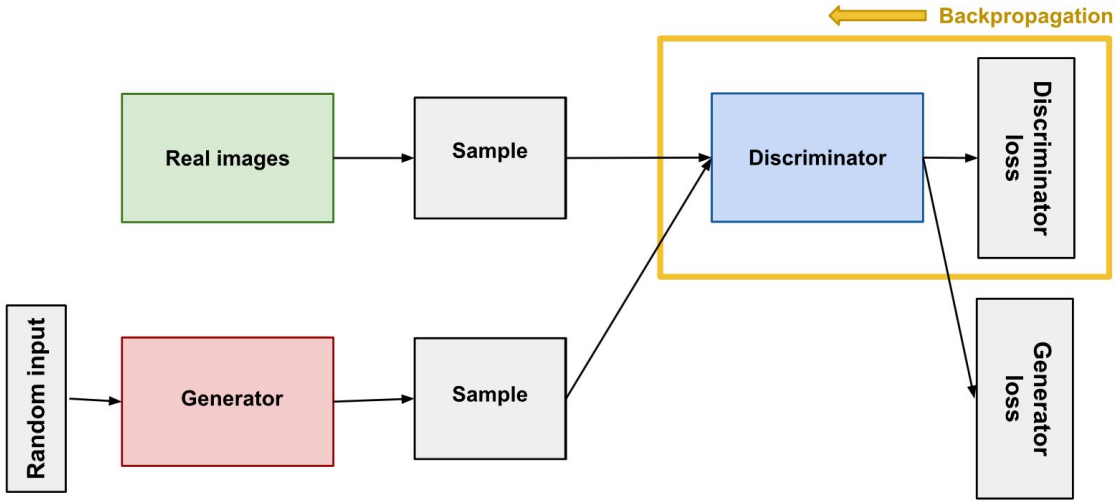
Generative Adversarial Network (GAN)

- GAN has two parts:
  - The **generator** learns to generate plausible data. The generated instances become negative training examples for the **discriminator**
  - The **discriminator** learns to distinguish the generator's fake data from real data. The **discriminator** penalizes the generator for producing implausible results.
- When training begins, the generator produces obviously fake data, and the discriminator quickly learns to tell that it's fake!



Generative Adversarial Network (GAN)

- The discriminator in a GAN is simply a classifier.
- It distinguished read data from data created by the generator.
- It could use any network architecture appropriate to the type of data it's classifying.



Generative Adversarial Network (GAN)

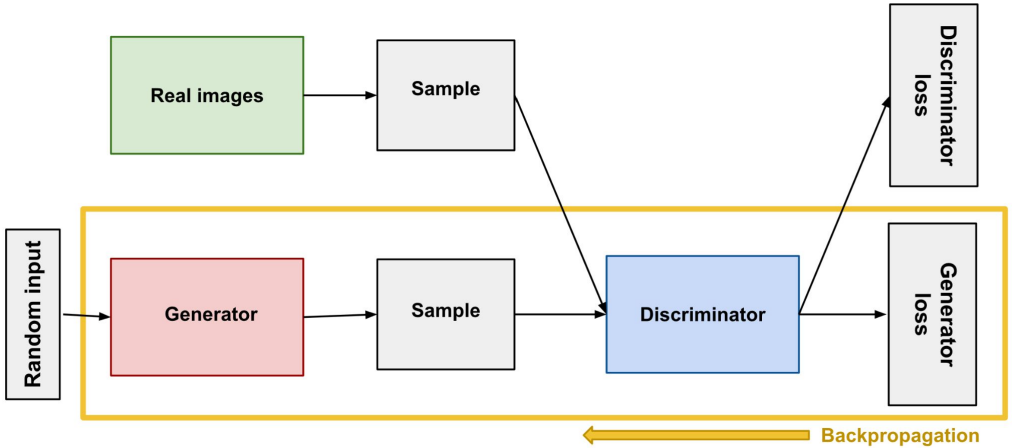
- The discriminator training data comes from two sources:
  - **Real data** instances, such as real pictures of people or real medical images. The discriminator uses these as positive examples during training.
  - **Fake data** instances created by the generator. The discriminator uses these as negative examples during training.
- The discriminator connects to two loss functions:
  - The discriminator classifies both real data and fake data from the generator
  - The discriminator loss penalizes the discriminator for misclassifying a real instance as fake or a fake instance as real.
  - The discriminator updates its weights through backpropagation from the discriminator loss through the discriminator network.
  -

Generative Adversarial Network (GAN)

- The generator learns to create fake data that can fool the discriminator
- Goal: Make the discriminator classify generator output as "real"
- Random Input (Noise):
  - Usually sampled from simple distribution (e.g., uniform)
  - Lower dimensional than output space
  - Enables diverse data generation
- Generator Network
  - Transforms random noise → meaningful data instances
  - By varying input noise → samples from different parts of target distribution
- Output
  - Synthetic data matching the format of real data
  - Should be indistinguishable from real samples

Generative Adversarial Network (GAN)

- Training the generator - Adversarial Training
  - Sample random noise
  - Generate fake data from noise
  - Pass fake data through discriminator
  - Get discriminator's "Real/Fake" classification
  - Calculate generator loss (penalized when discriminator correctly identifies fakes)
  - Backpropagate through BOTH networks
  - Update ONLY generator weights



Adversarial Training Dynamics and Convergence

- Two players: Generator (G) vs Discriminator (D)
- Alternating updates:
  - Train D (keep G fixed) → D learns G's flaws
  - Train G (keep D fixed) → G learns to fool a stationary D
- Why alternate? Prevents G from chasing a moving target; turns a hard generation task into solvable classification steps.
- Bootstrapping: if D can't beat random on G's early (bad) samples, training can't get started.
- Convergence behavior: as G improves, D's accuracy → ~50% (can't tell real vs fake). After this point D's feedback becomes noise → risk of G quality collapse.
- In practice, GAN "convergence" is often brief/unstable; monitor and stop before feedback degrades.

Common GAN Problems

- Vanishing gradients
  - What happens: D gets too good → G gets almost no learning signal.
  - Tries: Wasserstein loss (WGAN); modified minimax (maximize log D(G(z))).
- Mode collapse
  - What happens: G maps many z's to the same few outputs; G/D chase each other and cycle.
  - Tries: Wasserstein loss (train D to optimality without killing gradients); Unrolled GANs (anticipate future D steps).
- Failure to converge / instability
  - What happens: oscillations or divergence instead of settling.
  - Tries: Regularization—add noise to D inputs; penalize D weights.

GANs in Medical Imaging

- Clinical need: CS-MRI speeds up scans by undersampling k-space, but classic sparsity methods struggle with detail, tuning, and speed. DAGAN brings a conditional GAN to de-aliasing for fast, high-quality recon.
- Key contributions: U-Net generator with skips; refinement learning for stability/speed; content loss (pixel, frequency, VGG) + adversarial; frequency-domain consistency; broad comparisons.
- Speed: ~0.2 s/CPU slice or ~5 ms/GPU slice → near real-time.

Why MR-to-CT Synthesis?

- Radiotherapy requires both MR and CT
  - MR: Tumor/organ segmentation
  - CT: Dose planning calculations
- Current workflow problems:
  - Dual scan burden (time, cost, patient comfort)
  - Registration errors between modalities
  - Spatial misalignment issues

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Traditional Workflow:
MR Scan → Registration → Treatment Planning
CT Scan ↗           ↘ Potential Errors

Proposed Solution:
MR Scan → Synthetic CT → Direct Planning
          (No registration needed)
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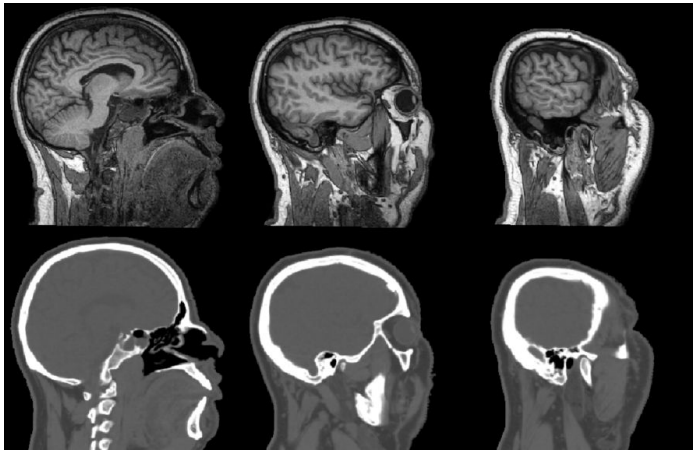
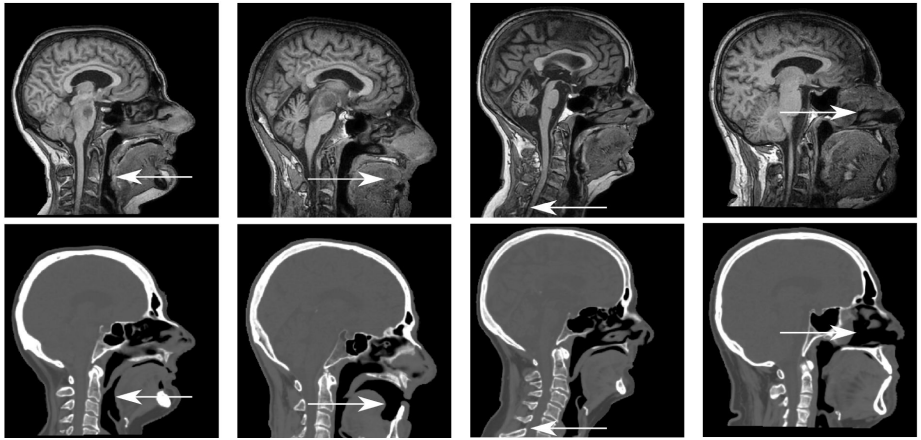


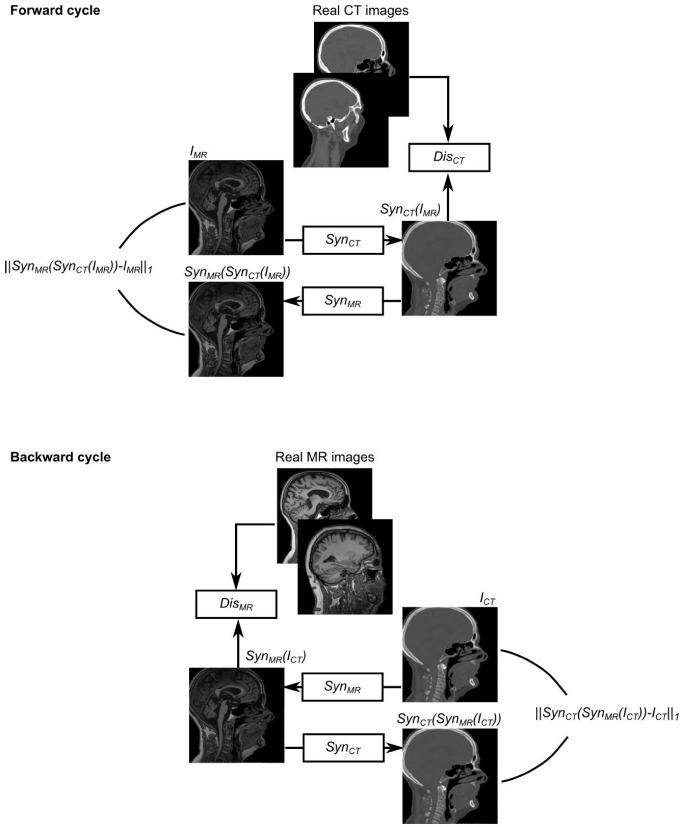
The Paired Training Problem

- Previous CNNs require paired training data
- Voxel-wise alignment assumption
- Problems with paired approaches:
  - Misalignment causes blurred synthesis
  - Limited training data availability
  - Cannot use unpaired clinical datasets



Bidirectional Translation with Cycle Consistency

- **Forward Cycle:**
  - SynCT: MR → CT synthesis
  - SynMR: CT → MR reconstruction
  - DisCT: Real vs. synthetic CT discrimination
- **Backward Cycle:**
  - SynMR: CT → MR synthesis
  - SynCT: MR → CT reconstruction
  - DisMR: Real vs. synthetic MR discrimination



CNN Components and Training

- **Synthesis Networks (SynCT, SynMR):**
  - 2 strided convolution layers
  - 9 residual blocks
  - 2 fractionally strided convolutions
  - Input/Output: 256×256 pixels
- **Discriminator Networks (DisCT, DisMR):**
  - PatchGAN architecture
  - 70×70 patch classification
  - Focus on high-frequency details

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Training Configuration:
- 18 patients (training)
- 6 patients (testing)
- 183 sagittal slices per volume
- Adam optimizer
- 200 epochs total
  - 100 with lr = 0.0002
  - 100 with linear decay
- λ = 10 for cycle consistency
- Training time: 52 hours (Titan X)
```

Adversarial and Cycle Consistency Losses

- **Adversarial Loss (CT):**

$$L_{CT} = (1 - Dis_{CT}(I_{CT}))^2 + Dis_{CT}(Syn_{CT}(I_{MR}))^2$$

- **Adversarial Loss (MR):**

$$L_{MR} = (1 - Dis_{MR}(I_{MR}))^2 + Dis_{MR}(Syn_{MR}(I_{CT}))^2$$

- **Cycle Consistency Loss:**

$$L_{Cycle} = ||Syn_{MR}(Syn_{CT}(I_{MR})) - I_{MR}||_1 + ||Syn_{CT}(Syn_{MR}(I_{CT})) - I_{CT}||_1$$

Competing Objectives:

Generator: Fool discriminator

Discriminator: Detect fakes

Cycle Loss: Preserve content

$$\text{Total Loss} = L_{Adv} + \lambda \cdot L_{Cycle}$$

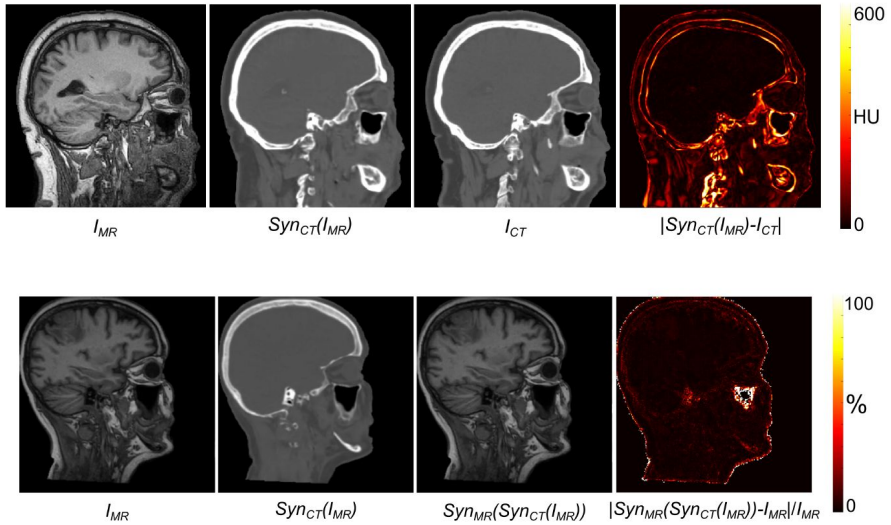
Quantitative Performance Comparison

- **Mean Absolute Error (MAE):**
  - Unpaired: 73.7 ± 2.3 HU
  - Paired: 89.4 ± 6.8 HU
  - 17.5% improvement
- **Peak Signal-to-Noise Ratio (PSNR):**
  - Unpaired: 32.3 ± 0.7
  - Paired: 30.6 ± 0.9
  - Higher is better
- **Statistical Significance:**
  - $p < 0.05$ (paired t-test)

	MAE		PSNR	
	Unpaired	Paired	Unpaired	Paired
Patient 1	70.3	86.2	31.1	29.3
Patient 2	76.2	98.8	32.1	30.1
Patient 3	75.5	96.9	32.9	30.1
Patient 4	75.2	86.0	32.9	31.7
Patient 5	72.0	81.7	32.3	31.2
Patient 6	73.0	87.0	32.5	30.9
Average ± SD	73.7 ± 2.3	89.4 ± 6.8	32.3 ± 0.7	30.6 ± 0.9

Synthesis Quality Comparison

- **Successful Differentiation:**
  - Bone vs. soft tissue
  - Ventricular fluid vs. air
  - Brain tissue structures
- **Error Distribution:**
  - Minimal in soft brain tissue
  - Higher in bone structures
  - Affected by neck misalignment
- **Unpaired vs. Paired:**
  - Less blurring with unpaired
  - Fewer artifacts
  - More realistic appearance



Accelerating MRI Acquisition

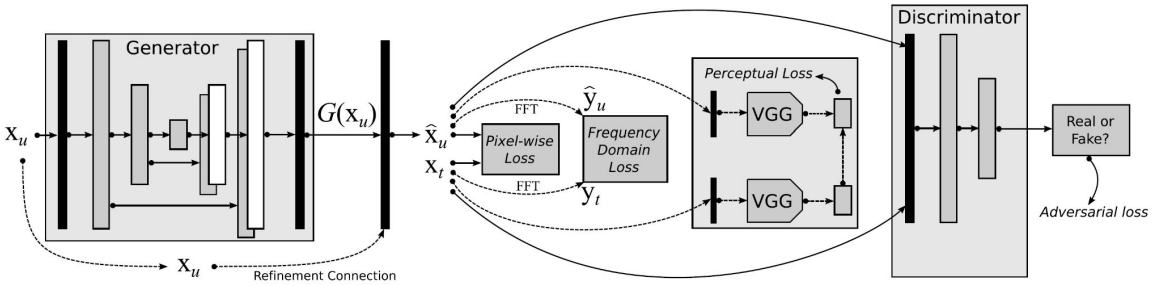
- **Problem:** MRI is inherently slow
  - Sequential k-space acquisition
  - 64-512 lines needed for quality
  - Patient discomfort, motion artifacts
  - High costs, contrast washout
- **Compressed Sensing Solution:**
  - Break Nyquist-Shannon barrier
  - Randomly undersample k-space
  - Exploit image sparsity
  - Acceleration factors: 2-6×

```
Traditional CS-MRI Pipeline:
k-space → Undersampling → Aliasing artifacts
          ↓
Iterative optimization (slow)
          ↓
Reconstructed image

DAGAN Pipeline:
k-space → Undersampling → Deep Network → 5ms
                                (trained offline)
```

Conditional GAN with Refinement Learning

- **Generator (U-Net):**
  - 8 encoder layers + 8 decoder layers
  - Skip connections preserve details
  - Refinement: G(xu) + xu (not just G(xu))
  - Stabilizes training dramatically
- **Discriminator:**
  - 11 convolutional layers
  - Distinguishes real vs. de-aliased
  - Provides adversarial feedback
- **Innovation:** Refinement learning
  - Generator learns missing information only
  - Reduces complexity, faster convergence



Multi-Component Loss Strategy

1. **Adversarial Loss (LGEN):**
   - Fool discriminator
   - Generate realistic images
2. **Pixel-wise MSE (LiMSE):**
   - Image domain fidelity
   - Preserve structural accuracy
3. **Frequency MSE (LfMSE):**
   - k-space consistency
   - Enforce data fidelity
4. **Perceptual Loss (LVGG):**
   - VGG network features
   - Preserve texture/edges
   - Prevent over-smoothing

```
LTOTAL = αLiMSE + βLfMSE + γLVGG + LGEN

Weights (balanced magnitudes):
- α = 15 (pixel loss)
- β = 0.1 (frequency loss)
- γ = 0.0025 (VGG loss)

Why this matters:
→ Adversarial alone: unstable
→ MSE alone: blurry
→ Combined: sharp, accurate
```

Performance Comparison

- **Undersampling Ratios Tested:**
  - 10%, 20%, 30%, 40%, 50% retained
  - (10×, 5×, 3.3×, 2.5×, 2× acceleration)
- **DAGAN Performance (30% retained):**
  - NMSE: 0.07±0.01
  - PSNR: 32.5±0.7 dB
  - SSIM: 0.87-0.98
- **Comparison vs. Others:**
  - TV: PSNR 28.2 dB
  - DLMRI: PSNR 28.5 dB
  - BM3D: PSNR 31.7 dB
  - **DAGAN: PSNR 32.8 dB**