

(3): Nuclear Oncology

* Many thanks to 431 team for their helpful notes *



Objectives

- *What are the tumor imaging and therapeutic radiopharmaceuticals?
- *What are the nuclear medicine tumor imaging methods?
- *What are the objectives of tumor imaging?
- *What are the potential values of nuclear medicine tumor imaging methods?
- *What is the role of nuclear medicine in the treatment of tumors?

Introduction

What is nuclear medicine?

Is a medical specialty involving the application of radioactive element which will be administered to the patient as an IV injection "most of the time" or orally" like iodine" and the gamma camera will detect the radiation emitting from the body. It is used:

- 1- To assess the function of the organs rather than the anatomy which is assessed by MRI and CT.
- 2- For diagnosis and treatment.

How to differentiate between radiology and nuclear medicine?

-in nuclear medicine: the machine"gamma camera" is detecting the radiation emitting from the patient -in radiology: the maching will give radiation to the patient

What is the role of nuclear medicine in oncology?

- 1-Diagnosis: specific or non-specific.
- 2-Staging: important for proper therapy.
- 3-Follow up: early detection for recurrence.
- 4-treatment: specific or non-specific.

Tumors "metabolic properties":

-Increased vascularization, Increased capillary permeability, Newly proliferated capillaries, Increased blood flow→Metabolically active"patient will lose weight"→ Increased energy demand.

Tumor cells "specific useful properties in imaging and therapy": (1)-High density of some common receptors, (2)Expression of several specific receptors and (3)Expression of some specific tumor antigenes.

Radioactive material

mainly two types: A-non-specific & B-specific

Note(s):

* In nuclear medicine, you need : <mark>Radioactive material</mark>

<mark>A gamma camera</mark> to detect the radiation.

*for each organ, there is a specific radiopharmaceutical agent, like -> if you want to scan the bone, you use the phosphate and you label it with a radioactive material

(A-1)-Tumor Non-specific **Diagnostic** radiopharmaceuticals "it can tell you

that there is a tumor but can't specify the type of the tumor which means Demonstrate tumor sites but are not specific for malignancy":

***PET or PET-CT /** 1-F-18 FDG(fluorodeoxyglucose) – anaerobic metabolism ***Planar, SPECT or SPECT-CT /**

1-Diphosphonates for bone scan

2-Ga-67 citrate – similar to FDG – localising agent

3-Tc99m Nanocolloid – bone marrow scan

4-Tc99m MIBI / Thallium 201 – several tumors

(A-2)- Tumor Non-specific therapeutic radiopharmaceuticals:
1- Sr-89(strontium-89)→used to treat bone metastasis+breast-CA +prostate CA,
2- Sm-153, Re-189 (all of them for Bone Palliation)

(B-1)-Tumor specific **Diagnostic** radiopharmaceuticals:(Binds directly to tumor antigens or receptors or are accumulated by special metabolic pathway) ***PET or PET/CT**

*Planner,SPECT or SPECT/CT

1-I-123/131 MIBG for neuroendocrine tumours

2- I-131 for differentiated thyroid carcinomas

3- **In-111** or **Tc99m** octreotide for tumours expressing somatostatin receptors. (Monoclonal antibodies labelled with In-111, I-123/131 or Tc-99m)

(B-2)-Tumor specific theraputic radiopharmacocutical :

1- I-131 to treat Thyroid cancer, as specific diagnostic if tumor significantly accumulates

2- Y(Yttrium)-90 Zevalin – monoclonal antibody for B-cell lymphomas

Physical Properties of Radionuclides

SPECT radionuclides stands for Single Photon Emission Computed Tomography

Radionuclide	T/2 physical	Type of radiation	E(kev)
-Technitium 99m(Tc-99m) diagnostic	6hrs	Gamma	140
-lodine I131 therapeutic	8days	Gamma/ Beta	364/606
-lodine I123 diagnostic	13.2hours	Gamma	159
-Gallium Citrate (Ga-67)	78.3 hours	Gamma	90,190,290
-Thallium Chloride 201 (Tl201)	73.1 hours	X-ray	68-83
-Indium 111 (In 111)	2.8 hours	Gamma	173,247
- Xenon 133	5.2 days	Gamma	81
-Kripton 81m	13 seconds	Gamma	190

*Note: if the radionuclide emits beta rays ightarrow it is therapeutic

PET radionuclides stands for Positron Emission Tomography

Radionuclide	T/2 physical	Positron energy	Productivity
-Fluorine 18	110 min	0.635	Accelerator

*Note: F-18 is the gold standard radiotracer used for tumor imaging together with glucose because tumor cells consume the glucose.

SUMMARY of the radionuclides

Non specific tumor imaging agents:

- •Tc-99m MDP bone scan: Detection and follow up of bone metastasis
- •Gallium 67 : Staging , Restaging & therapy assessment of HD , NHL , Lung cancer

•Thallium 201 : Tumor viability & tumor seeking.

{Tc-99 m Agents (MIBI ,TETRO.).}

•F18 – FDG : Staging , Restaging & therapy assessment of HD , NHL , Lung cancer

Specific tumor imaging agents:

•In-111 (TC99m) Octreotide : Neuroendocrine tumors

- •I -123 MIBG : Neuroendocrine tumor
- •I -131 : Lung mets. thyroid carcinoma

What are the nuclear medicine tumor imaging methods?

1-conventional tumor imaging

A-Planner B-SPECT C-SPECT/CT

2-Onco PET

A-PET B-PET/CT

"ALL systems are at KKUH except PET"

Examples:

A-planner imaging "means only 2-dimensions,axial+perpendicular"

Anterior

Growth plate

-This is the whole body bone scan -This is how the normal body looks like -If the growth plates look very radioactive->young patient

Posterior

B-SPECT and SPECT/CT "here, a Patient with hodgkin lymphoma and ant. Medistinal uptake"



Only SPECT without CT, It can tell us if there is any abnormal uptake of the tracer.



1st row/SPECT (shows abnormal uptake) 2nd row/CT (only shows the location-> ant.mediastinum) 3rdrow/SPECT+CT (abnormal uptake in the ant.mediastinum) +<mark>3D image</mark>

C-PET and PET/CT: " here, we gave the patient glucose labeled with a radioactive material which was F-18, to see any area with high glucose turnover like muscles"



PET scan



1st-CT 2nd-PET 3rd-PET/CT

Note(s):

A-In the PET/CT image above, we can see the heart very clearly and this means that the heart is deriving energy from glucose which is labeled with the radioactive material-> this happens in post-prandial phase

B-In fasting phase-> heart derives energy from the fatty acids

Bone Scan

Radiopharmaceuticals

Technitium 99m Methylene DiPhosPhonate (Tc-99m MDP)

- •Tissue accumulation depends on
- -blood flow
- -capillary permeability
- -metabolic activity of osteoblasts and osteoclasts

-mineral turnover

• Dose: 500 to 800 MBq (Megabequerel) / 15- 20 mCi (millicurie)

•Imaging time: 2 to 3 hours postinjection – WB + SPECT

•Potentials of bone scan: Positivity many months before an abnormality can be detected on X ray

Its indications

I- Metastatic Disease: Lung cancer, prostate, breast, thyroid, and renal tumours

- ✗ Diagnosis.
- ✗ Initial staging.
- ✗ Restaging.
- ***** Asses response to therapy.

II- Primary Bone Tumors :

- ✗ Malignant or Benign
- Therapy planning for patients with primary bone malignancy (e.g. Osteogenic & Ewings sarcoma)

III- Soft tissue tumors : (if the bones are involved or not)

- * Primary
- ✗ Metastases

A-Bone scan in oncology "imaging features":

Hot lesions (take the tracer)	Cold lesion	Super- scan	Normal distribution	Soft tissue uptake	Flare phenomenon
-Majority of bone tumors	-Appears as a defect. - Purely osteolytic tumors (renal cell carcinoma, thyroid cancer, anaplastic tumors),radiation therapy	-if the metastasis is widespread. - Diffuse increased skeletal uptake with no soft tissue or kidney activity (e.g. CA prostate ,breast ,etc).	Bone Marrow tumors (e.g. lymphomas, leukemia, multiple myeloma). (it appears normal-> inside the bone)	-Soft tissue tumors may concentrate the tracer. (because of the blood supply->the tracer might reach soft tissues)	increased number of lesions in the case of effective therapy (there will be an osteoplastic reaction to heal the bone metastasis, so if you repeat the bone scan, you will see hot lesions ->and it is a good sign).

Note(s):

Flare phenomenon or **osteoblastic flare phenomenon** refers to interval visualisation of lesions with a sclerotic rim around an initially lytic lesion or sclerosis of lesions previously undetected on radiograph or CT in the setting of follow up of an oncological patient with other signs of partial response to treatment. It does not indicate disease progression but the healing of previously inconspicuous lesions.

B-Normal whole body bone scan:



An 8-year-old child.(with radioactive growth plates and costochondral junctions)



A 25-year-old adult



C- an example of bone metastasis:

CA-breast (you can see multiple spots in the skull spine and ribs)



CA-Prostate (you can see multiple spots in proximal femurs, whole spine, ribs, proximal humerus, and scapula)



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D- Super-scan (diffuse involvement):

Definition : Bone scan with diffuse symmetrical increased uptake and almost absence of soft tissue activity, lack of kidney activity and bone uptake seen in blood pool images.

Causes :

- Bone metastases : Prostate, breast, lung, bladder and lymphoma.
- Non tumor causes: HPT(hyperparathyroidism), osteomalacia, Pagets disease and fibrous dysplasia (metabolic bone disease)

Important clues:

In metabolic bone disease the calvarium(skull) and long bones are involved unlike in bone metastases.

Note(s):

How to differentiate between the metastasis and metabolic bone diseases?

In mets only the axial bones are affected while in metabolic bone disease all the bones are affected either axial or horizontal.

Example:





Pure lytic lesions: (cold lesions)





Pure lytic tumor (you can see the defect in the spine)

Note(s):

Pure lytic lesion means when the tumor metastasize, there will be no osteoplastic reaction around it to heal the lesion.

Ewing's sarcoma:



Primary tumor localized to the left proximal femur without metastasis.



The tumor can bee seen in the x-ray but we do the bone scan to see if there is any metastasis. (Here, no metastasis)

Nuclear Medicine



Osteoid Osteoma: (Primary benign bone tumor, commonly found in children, characterized by night pain that is relived by aspirin)



Osteoid osteoma Localized in the mid-shaft of right tibia -the 3 stage bone scan shows: increase blood flow, blood pool and tracer uptake

Giant cell tumor:



Giant cell tumor can be seen in x-ray and MRI but the objective of the whole body scan is to see if there is any other lesions.



It is localized to the right proximal tibia

Soft tissue sarcoma:

In soft tissue tumors, we want to see if there is:

- 1- An extension to the underlying bones
- 2- Or a distant metastasis.



In the 3 stage bone scan you can see the lesion is vascular with high blood pool and the underlying (right femur) bone is intact \rightarrow because here only the underlying cortex is affected not the whole bone also, the rest of the skeleton is intact.

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ANTERIOR

Uses of Gallium Scan in Lymphomas:

- Staging
- Follow up and monitoring of therapy
- Detection of tumor recurrence
- Differentiate post-therapy changes: tissue necrosis and fibrosis from local recurrence.

The Gold Standard for tumor-imaging and lymphoma is Flourine-18 but the Gallium can be used instead of it What is seen in the image? The black spots are enlarged lymph nodes: in the neck, mediastinal, par-aortic, axillary, and iliac (Stage IV cuz above and below the diaphragm)

A) Prediction of response to therapy

Normalization of a positive pre-therapy scan: A negative scan after one cycle or at mid cycle is associated with a high likelihood of complete response. Patient with primary lymphoma in the mediastina and epigastric regions. Pre and post-chemotherapy showed excellent response so it is used here to know if it is responsive and complete the treatment or not.

B) Prediction of outcome

Residual gallium uptake after treatment is a poor prognostic sign, indicates viable tumor and treatment should be modified. The response is not good cuz the uptake is almost the same pre and post-chemotherapy. After the first dose of chemo you wait 2 weeks and do Gallium, if residual, go to other plan of chemo.



ANTERTOR



Gallium Scan NHL: SPECT CT



It determines precisely the size and locality. The image is for lymphoma patient in the anterior mediastina. Nowadays, they always order it. Soon, the Gallium won't be used anymore and it will be replaced by the PET.

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Ga-67 SPECT/CT: Staging HD

Abnormal Ga uptake (a) in supraclavicular, axillary, Paratracheal , parahilar and para-aortic lymph nodes and in the spleen, at lesion sites corresponding to those observed on CT. The para-aortic lymph node uptake (b) combined with CT findings allowed the diagnosis of subdiaphragmatic disease and excluding bowel activity.

Neuroendocrine Tumors:

- In-111 octreoscan.
- ♦ I123 MIBG Scan.

Somatostatin Receptor Imaging

A) Indium-111 Octreoscan: Insulinoma

It is metabolized in the liver, concentrated in spleen and excreted by the kidneys

Clinical History:

The patient is a 66-ys male with insulinoma, now being evaluated for evidence of recurrent and/or metastatic disease.

Findings :

Multiple lung, mediastinum, liver and abdominal metastases.

B) I123 MIBG Scan : Meta Iodo Benzyl Guanidine

- Is a nor adrenaline analog
- Localizes in adrenergic tissues: catecholamines producing tumors

and their metastases.

 Patient preparation: stop drugs interfering with MIBG uptake.
 Lugols solution to protect thyroid gland

Indications:

- Pheochromocytoma
- Paraganglioma
- Insulinoma
- Neuroblastoma
- Medullary thyroid carcinoma
- Carcinoid tumors











Planar Vs. SPECT CT:

A 41 years old female patient is with 2ndary hypertension. Right adrenal mass "Pheochromocytoma" It show more localization and size in the right para-spinal area above the adrenal gland near the vertebra





Neuroblastoma

It is a tumor that affects the children under 5-years. MIBG would tell if it is a primary and if there is a metastasis. This patient has no metastasis, only the primary mas in the abdomen anterior to the spine

Planar Vs. SPECT CT:



1ry neuoroblastoma with bone metastasis:



How do you know it is a tibia? by correlating it with the X-ray >>

<< 1ry Abdomenl mass



THYROID METASTASES STUDY:

(I-123 or I-131 as Sodium Iodide) Diagnostic and therapeutic

Indications:

Detection and localization of persistent or recurrent local or distant functioning thyroid cancer

Patient Preparation:

• Stimulation of potentially functioning thyroid tissue:

A. Inject recombinant human thyrotropin on 2 consecutive days and administer the iodine on the third day .

- B. Withdraw thyroid replacement hormones :
 - 1. Thyroxine (T-4) for at least 4 weeks.
 - 2. Triiodothyronine (T-3) for at least 10 days.
- The patient must not have had i.v iodinated contrast material (IVP, CT with contrast, myelogram, angiogram) for at least 3 weeks .
- The patient should be NPO for at least 4 hours prior to radiopharmaceutical administration and for at least 1 hour afterwards .

Tracer, Dose, & Technique of Administration:

Radiopharmaceutical: Oral administration

- a. I-123 as sodium iodide : 2 mCi
- b. I-131 as sodium iodide : 2-10 mCi

Imaging using Gamma camera: Whole body scan



Negative I-123 WB Scan



I-123 WB Scan: Post-operative

Thyroid remnants



I-123-scan: Patient with recurrent thyroid cancer and metastasis to the anterior mediastina "Planar Vs. SPECT CT"



Local ecurrence

Bone metastasis

(I-123 or I-131 as Sodium iodide)

Lung metastasis

I-131 Pre & Post therapy



>Dec04



Onco PET (PET and PET CT)

- PET : Positron Emission Tomography.
- CT : Computerized Tomography.
- PET-CT is the fusion of functional and anatomic information acquired almost simultaneously from which we are able to visualize form and function.

Nuclear Medicine

432RadiologyTeam



Scan

Corrected PET Emission Scan

Fusion Scan

Corrected (NAC) Emission Scan

Detector

Detector

PET CT = PET + CT = Function + Form

PET : How it is performed...? Skipped by the Dr

Positron emitters (e.g. F18) labelled with biologically active natural compounds such as oxygen, carbon or glucose give intravenously and reacting in the body identically to their non-radioactive counterparts. Positrons are emitted from F18 and react with tissue electrons.....Anhillation occurs... Two photons 511 kev each in opposite direction are emitted and detected by PET SCANNER giving an image of the normal and abnormal distribution of tracer in the body.

Cyclotron produced isotopes:

Isotope	T/2
Oxygen-15	2 min
Nitrogen-13	10 min
Carbon-11	20 min
Fluorine-18	110 min

FDG in Oncology: Skipped

- Tumors do not have a blood tumor barrier
- FDG transport into tumors occurs at a *higher* rate than in the surrounding normal tissues.
- ◆ FDG is de-phosphorylated and can then leave the cell.
- The de-phosphorylation occurs at a *slower* rate in tumors.

Applications of FDG:

- Locating unknown primaries
- Differentiation of tumor from normal tissue
- Pre-operative staging of disease (lung, breast, colorectal, melanoma, H&N, pancreas)
- Recurrence vs. necrosis
- Recurrence vs. post-operative changes (limitations with FDG)
- Monitoring response to therapy

F18 FDG IMAGING PROTOCOL:

♣ Fasting : 4 – 6 hours

- Dose : Inject 10 mCi F18 FDG
- ♣ Wait (uptake phase): 45 -60 min then scan
- Scanning time : 30 min to complete PET CT study
- SUV : Standard uptake value (N:0.5-2.5 and Tumors > 3.0)



>FDG PET-CT : Normal and abdomen

FDG PET-CT: Staging NHL< lymph nodes in mediastina

FDG PET





Brain has high metabolic rate so it's normally black and so, the PET has low sensitivity for brain tumors

Assessment of therapy response: FDG PET in HD







Post therapy

A 22 years old male patient with Hodgkin's lymphoma. Six months after chemotherapy, CT scan showed bilateral hilar abnormalities. FDG-PET scan did not show any activity in described CT changes. Very good response!

FDG in Non-Hodgkin's lymphoma: Response to therapy (Skipped)



PET CT in Lymphoma (Skipped)

	Specificity (%)	Sensitivity (%)
СТ	89	61
FDG-PET	98	78
FDG-PET and CT	99	91
FDG-PET/CT	99	96

PET CT: Lung cancer staging



FDG avid soft tissue mass associated with a destructive L5 spinous process consistent with metastatic deposit (arrow: one vertebra). FDG PET CT in Solitary Pulmonary Nodule (SPN): *Sensitivity : 82 – 100 % *Specificity : 67 – 100 %

PET CT: Rectal cancer staging



A 57-year-old woman presented with pain and constipation and colonoscopy revealed an obstructing rectal mass. A staging FDG-PET/CT demonstrated intense FDG avidity in a circumscribed mass-like thickening of the proximal rectum (arrows in top row images) and a focus of mild metabolic activity anterior to the rectum (bottom row arrow) which was not avid as the rectal malignancy. This was located within the uterus as seen on CT images (bottom row), and was subsequently shown to be a uterine fibroid on other imaging studies.

PET CT: Esophageal cancer staging



Based on FDG-PET/CT results the clinical management of this patient was changed from surgical resection of the primary tumor to combined chemo-radiation therapy (Axillary lymph nodes met)



FDG PET: Tumor of unknown origin (Skipped)

Pharyngeal cancer

Metastatic involvment of neck lymph nodes

FDG PET - brain tumor: post therapy Two foci on CT, only one viable tumor



Similar to the filling defect

Indications of PET CT:

Breast Cancer*	Staging*, restaging*, and monitoring response to therapy*
Colorectal Cancer	Diagnosis*, staging* and restaging*
Esophageal Cancer	Diagnosis*, staging* and restaging*
Head & Neck Cancers (excluding CNS and thyroid)	Diagnosis*, staging* and restaging*
Lung Cancer (Non-Small Cell)	Diagnosis*, staging* and restaging*
Lymphoma	Diagnosis*, staging* and restaging*
Melanoma (Excludes evaluation of regional nodes)	Diagnosis*, staging* and restaging*
Solitary Pulmonary Nodule	Characterization of indeterminate single pulmonary nodule
Thyroid Cancer*	Restaging
Cervical Cancer*	Staging as an adjunct to conventional imaging

Radionuclide Therapy: Properties of the Ideal Therapeutic Radiopharmaceutical

- 1. Pure beta minus emitter
- 2. Medium/high energy (>1 meV).
- 3. Effective half-life = moderately long, e.g., days.
- 4. High target:nontarget ratio
- 5. Minimal radiation dose to patient and Nuclear Medicine personnel
- 6. Patient Safety
- 7. Inexpensive, readily available radiopharmaceutical.
- 8. Simple preparation and quality control if manufactured in house.

Radionuclide Therapy

Agent	Indication	Dose
I-131	Thyroid cancer	100-200 mci
132 MIBG	Neuroblastoma	100-300 mCi
Strontium	Bone metastasis	40-60uCi/kg
Sm-153-EDTMP		1.0 mCi per kg
Phosphorus- 32	P olycythaemia	2.3mCi/m2
Y-90-Ibritumomab Tiuxetan [Zevalin®]	B-Cell NHL	Y-90-ibritumomab tiuxetan. > Platelet count > 150,000 cells/mL: 0.4 mCi/kg > Platelet count 100,000-150,000 cells/mL: 0.3 mCi/kg The dose should never exceed 32 mCi (1,184 MBq).

Strontium-89 Therapy for Palliation of Bony Metastases



History : A 65 Ys ,M, with CA prostate and widespread bone metastases and severe bony pain. Admitted for palliative Strontium-89 therapy. Procedure :

- •Bone metastases was confirmed by bone scan.
- •The patient was given 40 mCi of Strontium-89 I.V.according to body weight of the patient.
- •The patient experienced one day of exacerpated pain which was controlled by opiates but the following day showed gradual pain relieve.

Teaching Points

NM tumor imaging:

- Functional
- Sensitive
- Whole body evaluation
- Specific : Some tumors
- Targeted therapy

Objectives of NM tumor imaging

- Diagnosis
- Staging
- •Guiding biopsy
- •Follow up and therapy monitoring
- •Detection of recurrence.

SUMMARY

Nuclear Medicine tumor imaging for:

•Diagnosis,Staging,Guiding biopsy, Follow up, therapy monitoring and Detecting recurrence.

Radionuclides

	Specific	Non-specific	
1) PET or PET CT.		1) PET or PET CT:	
		*F-18 FDG (Gold standard & the most used). T/2: 110 minutes	
2) Planar, SPECT or	SPECT-CT		
		2) Planar, SPECT or SPECT-CT:	
*I-123/131 MIBG	Neuroendocrine tumors	*Diphosphonates	Bone scan
*1 101	Differentiated thyroid	*Co 67 citrato	Similar to EDG
1-151	carcinomas	Ga-67 citrate	Similar to FDG – localizing agent.
*In 111 or To00m	Tumors expressing	*T-90m Nanacallaid	Pana marraw scans
-11-111 of 1699m	somatostatin receptors		Bone marrow scans.
*Monoclonal antibodies labelled with In-111, I-123/131 or Tc-99m.		*Tc99m MIBI / Thallium 201 Several t	Soveral tumora
			Several tumors.

Therapeutic radionuclides

Specific	Non-specific
I-131:	Sr-89, Sm-153, Re-189:
Thyroid cancer, as specific diagnostic if tumor significantly accumulates.	Bone pain palliation (used to treat bone metastasis
Y-90:	
Zevalin – monoclonal antibody for B-cell lymphomas.	

Half life of radionuclides:

- Tc- 99m:6 hours
- I- 131:8 days (used for therapy)
- I- 123:13.2 hours
- Ga- 67: 78.3 hours

Nuclear Medicine

Questions

- 1) A 65 yo male patient with prostatic
- 2) enlargement and elevated PSA.
- 3) Bone scan requested and revealed ?
 - a. Osteoprosis with multiple fractures.
 - b. Osteoarthritis of the spine.
 - c. Bone Metastasis.
 - d. Urinary bladder tumor.



4) Brown tumor and subperiosteal bone resorption are associated with?

- a. Hyperthyrodism.
- b. Scleroderma.
- c. Hyperparathyrodism.
- d. Rheumatoid arthritis.
- 5) A 20 yo male patient with suspected lymphoma. What is the following and what's showing.



- a. Tc-99m MDP bone scan with multiple bone metastases.
- b. F-18 PET scan with multiple lymph node metastases.
- c. Ga-67 scan with multiple Lymph node metastases.
- d. I-131nwole body scan with multiple Lymph Node Metastases

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Answers:
1st Questions:c
2nd Questions:c
3rd Questions:c