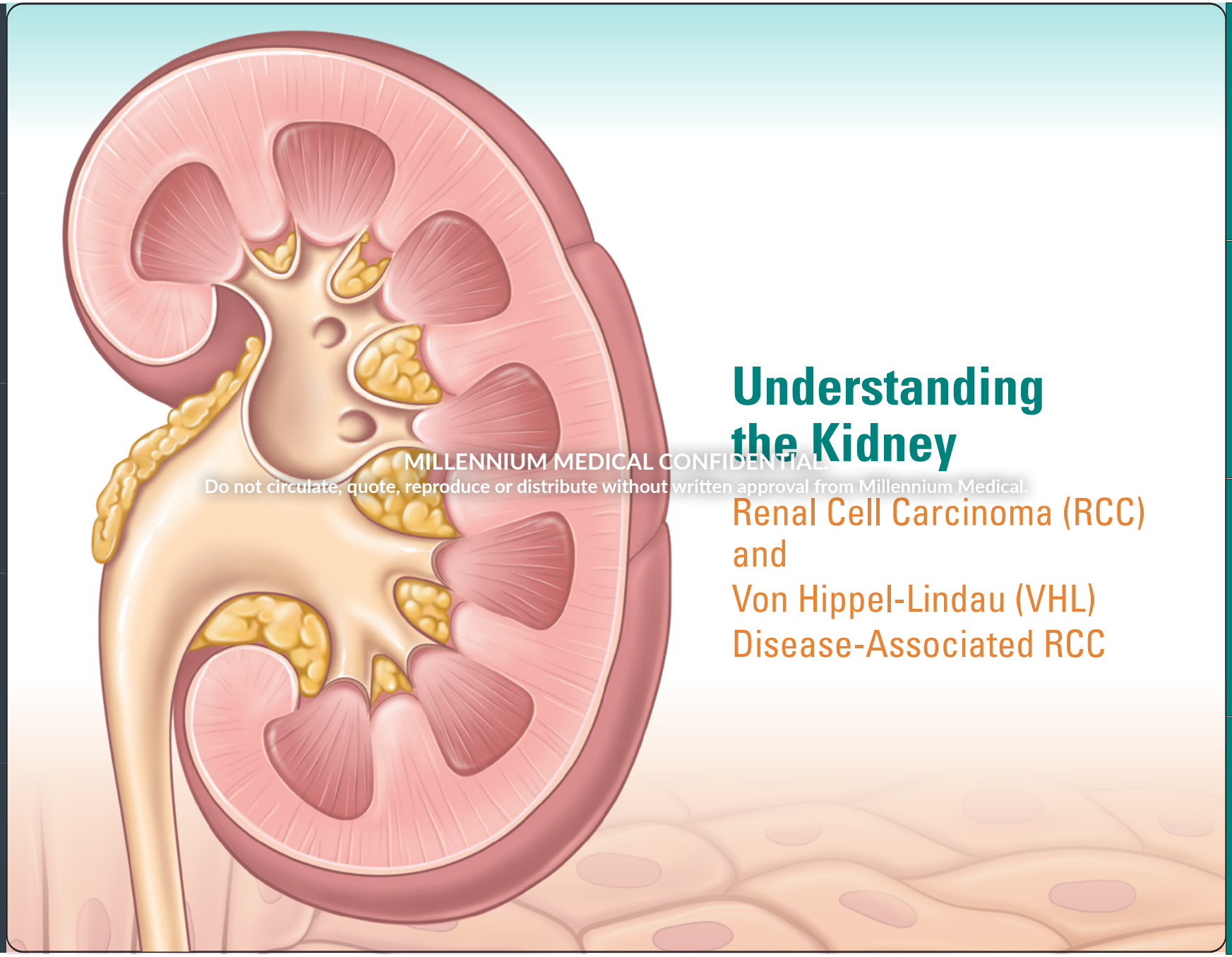
The Kidneys and How They Work

Kidney Cancer Overview

Types of RCC

Classifying RCC

RCC Stages



Understanding the Kidney

Renal Cell Carcinoma (RCC) and Von Hippel-Lindau (VHL) Disease-Associated RCC

Care Team and Treatments

Primary Treatments

Living with Cancer

VHL Disease-Associated RCC

FRONT COVER

The Kidneys and How They Work

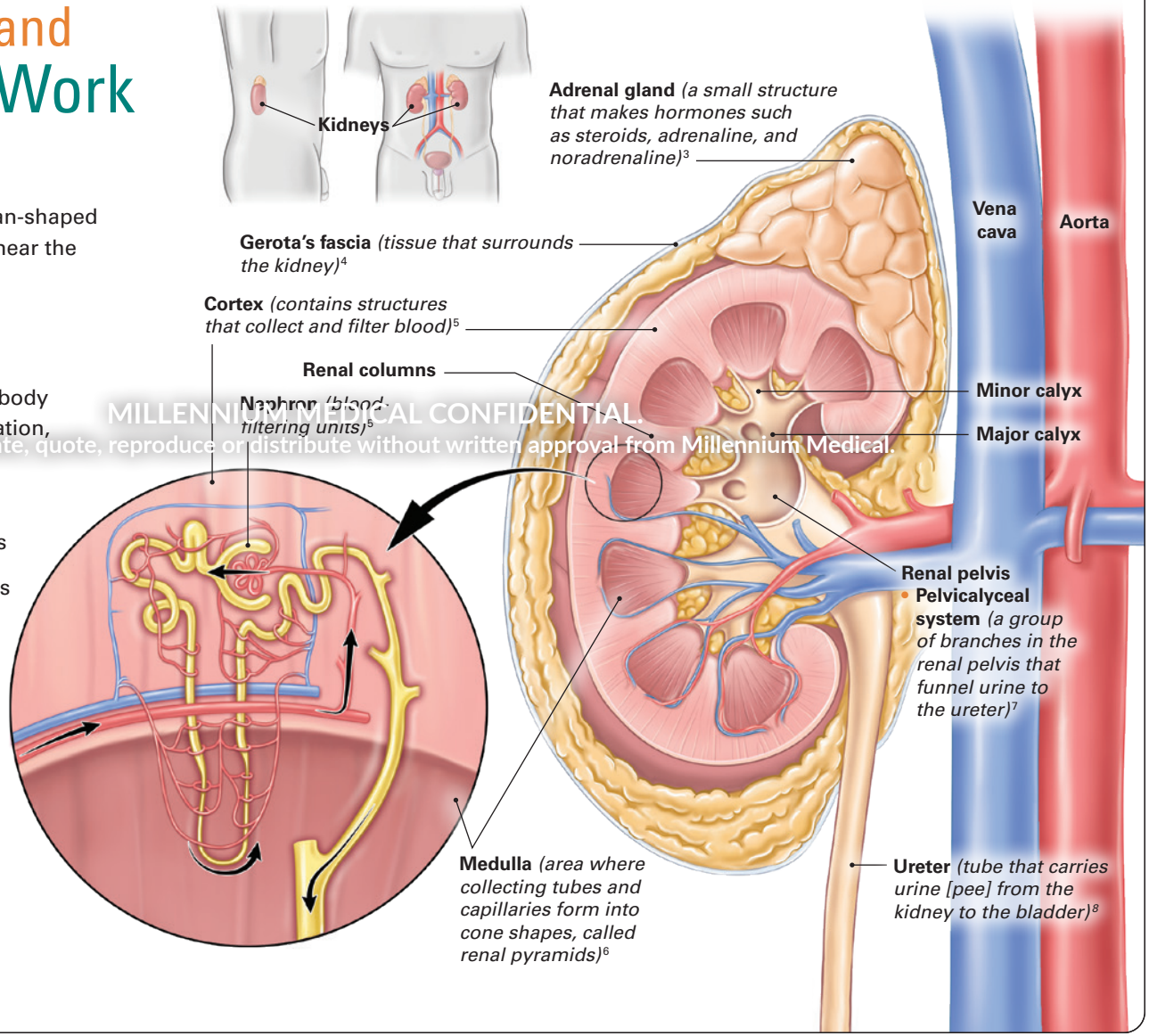
The **kidneys** are a pair of bean-shaped organs behind the stomach near the lower back.[1]

What the Kidneys Do[2]

The kidneys main job in the body is to **filter blood**. During filtration, the kidneys:

- Remove waste
- Regulate salt concentrations
- Maintain proper water levels

They also help control certain hormones that regulate blood pressure and red blood cell formation.



Kidney Cancer Overview

Kidney cancer is one of the 10 most common cancers in males and females. It is more common in **older adults** between 65 and 74 years old.[9] Renal cell carcinoma (RCC) is the most common type of kidney cancer. About 9 out of 10 kidney cancers are RCC.[10]

Some Risk Factors[11]

Some **risk factors** may raise the chance of developing kidney cancer. These include:

- Smoking
- Obesity
- High blood pressure
- Family history of kidney cancer
- Exposure to chemicals
- Sex assigned at birth (higher incidence among males)
- Race
- Advanced kidney disease
- Genetic risk factors you inherit from a parent

Signs and Symptoms[12]

Having one or more of these may be signs of kidney cancer:

- Blood in the urine
- Lower back pain (one-sided)
- Feeling tired
- Loss of appetite, possibly causing weight loss
- Anemia
- Unexplained fever

Anemia is when you have a lower than normal amount of red blood cells[13]

Determining Risk[14]

Prognostic, or risk models, are **statistical** tools that factor a patient's kidney cancer **characteristics**. They may help guide treatment decisions.

Disclaimer: These models are not mandatory to use. Your provider will discuss what may be best for you.

Tests to Detect Kidney Cancer

Proper diagnosis of kidney cancer depends on **tissue samples** or microscope images.[15]

Scans of the kidney and surrounding area can also be helpful in diagnosing cancer. You may need one or more of the following[15]:

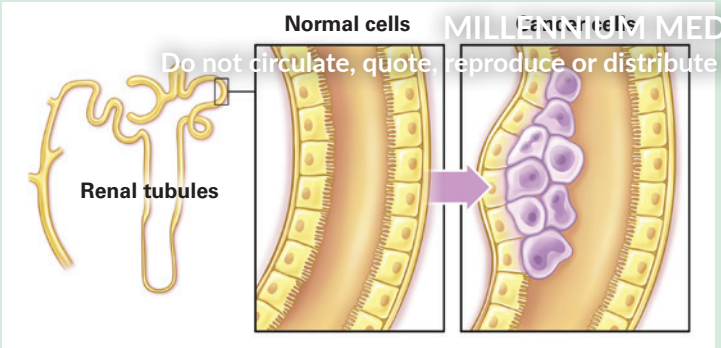
- **Computed tomography (CT) scan**: a computerized scan that takes 3-dimensional pictures of tissues and organs[16]
- **Magnetic resonance imaging (MRI)**: a scan that takes detailed pictures of tissues and organs, mostly helpful for soft tissues[17]
- **Ultrasound**: a scan that uses sound waves to create pictures of tissues and organs inside the body[18]
- **Angiography**: an X-ray scan that looks at blood vessels[19]

Primary lab tests, such as blood and urine, are not able to diagnose kidney cancer, but they may be helpful in discovering a problem with the kidney.[15]

Types of Renal Cell Carcinoma (RCC)

Renal Cell Carcinoma (RCC)[10]

- The most common form of kidney cancer is renal cell carcinoma (RCC), which is cancer that starts in the cells that line the **renal tubules**
- Nearly 9 out of 10 kidney cancers are RCCs



Clear Cell Renal Cell Carcinoma (ccRCC)[2]

- One type of RCC is known as clear cell renal cell carcinoma (ccRCC) since cells appear clear under a microscope
- About 7 out of 10 people with RCC have ccRCC, making it the most common type of RCC

Non-Clear Cell Renal Cell Carcinoma (nccRCC)[2,10,20]

- Several types of nccRCC include:
  - **Chromophobe**: cancer cells are pale and larger than clear cells
  - **Papillary**: cancer cells form finger-like projections (papillae)
  - **Collecting duct RCC**: cancer cells form in the collecting ducts or tubules
  - **Multilocular cystic RCC**: cancer cells form small cysts, fluid-filled sacs
  - **Unclassified**: cancer cells do not look like other types

Classifying RCC

Classifying RCC depends on several factors such as tumor size, location, how aggressive tumor growth is, and lymph node involvement. Cancers can be classified based on their stage, grade, and other characteristics.[15,21]

Cancer Stage[21]

Cancer stage describes how much cancer is in the body and where it is located. The TNM system is used to determine the stage of RCC. It is based on 3 parts:

T = Primary Tumor

- How large is the tumor?
- How invasive is the tumor?

N = Regional Lymph Nodes

- Has the cancer spread to nearby lymph nodes?

M = Distant Metastasis

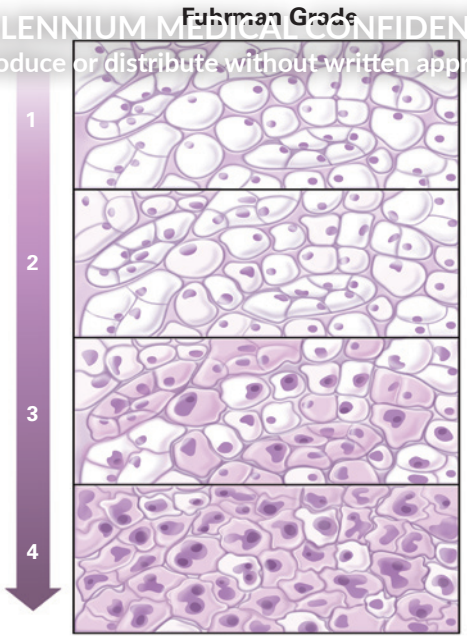
- Has the cancer spread to other organs?

Cancer Grade

The grade describes how normal or abnormal the cells look under a microscope. The more abnormal cells look, the more aggressive the cancer is and the faster it is likely to grow and spread.[22]

Fuhrman Grade: a value on a scale of 1 to 4 given to RCC cells indicating aggressiveness.[15]

- **Grade 1** cells tend to grow **slowly** and appear more like normal cells while **grade 4** cells are more **aggressive** and usually appear abnormal[15]



WHO*/ISUP Grade**: a newer system that grades on the **highest-grade cells present**, not the most predominant.[23]

Other Characteristics on the Pathology Report

Characteristics of the kidney tissue sample, or histology, can help classify the cancer.[21]

The two main histological types of RCC are[21]:

- **Sarcomatoid:** highly aggressive[10]
- **Rhabdoid:** usually linked to poor outcomes[21]

Molecular Pathology is done to check for clues from tissue, blood, or bodily fluid samples that may indicate unusual kidney function.[24]

Surrogate Endpoints help classify cancer by looking for signs that indicate tumor growth, functioning, and how well the tumor might respond to treatment.[25]

Looking for signs of **necrosis**, or cell injury causing permanent damage, can also help in classification of tumors.[26]

*WHO: World Health Organization

**ISUP: International Society of Urologic Pathology

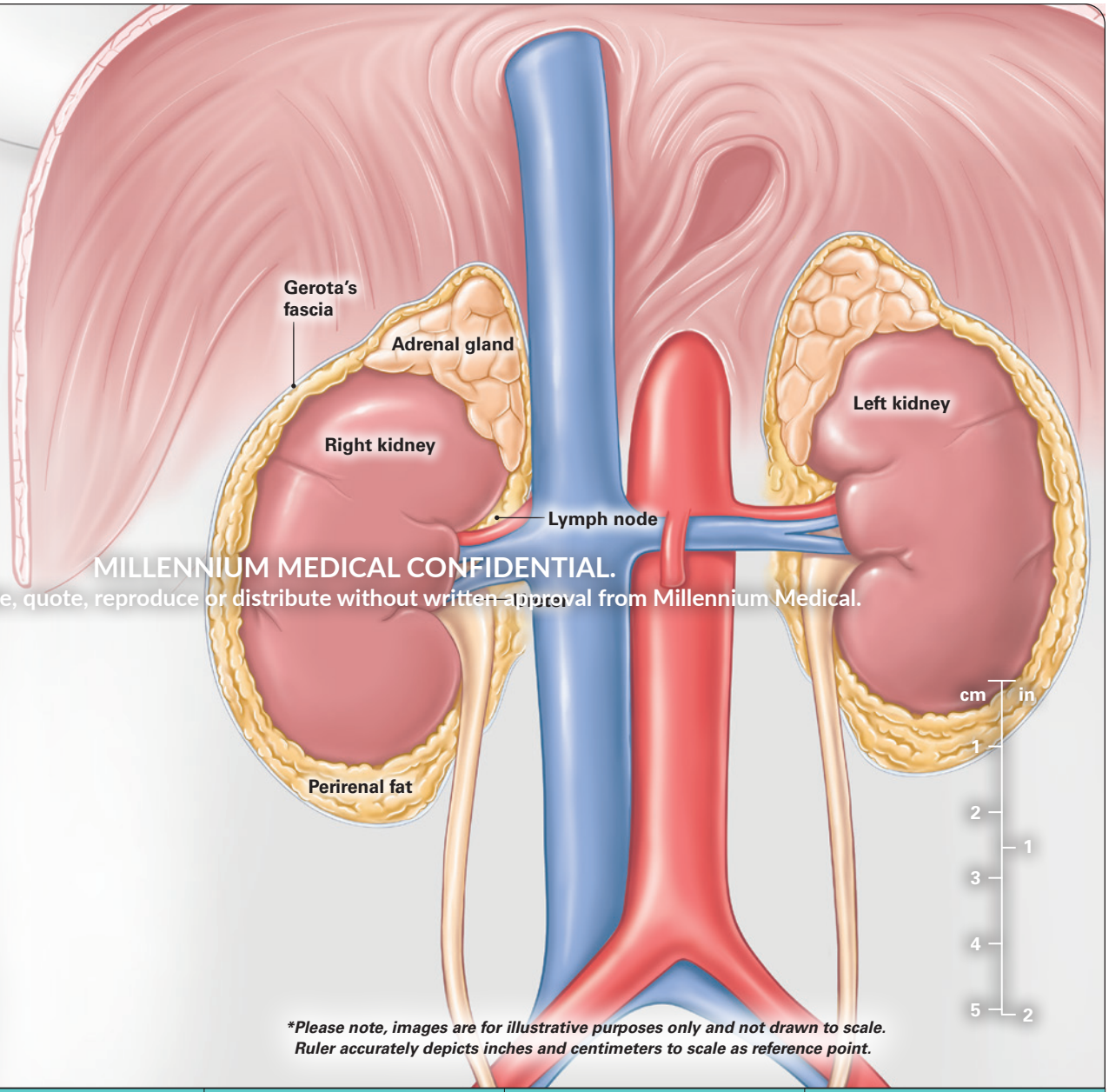
RCC Stages[21]

Staging of RCC is determined by several factors.

Tx, T0

Tumor undetectable

- **Tx**: Primary tumor cannot be assessed
- **T0**: No evidence of primary tumor



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RCC Stages

Tx, T0	T1	T2	T3	T4

COMPOSITE

Stages Tx, T0–T4

RCC Stages[21]

Staging of RCC is determined by several factors.

Tx, T0

Tumor undetectable

- **Tx**: Primary tumor cannot be assessed
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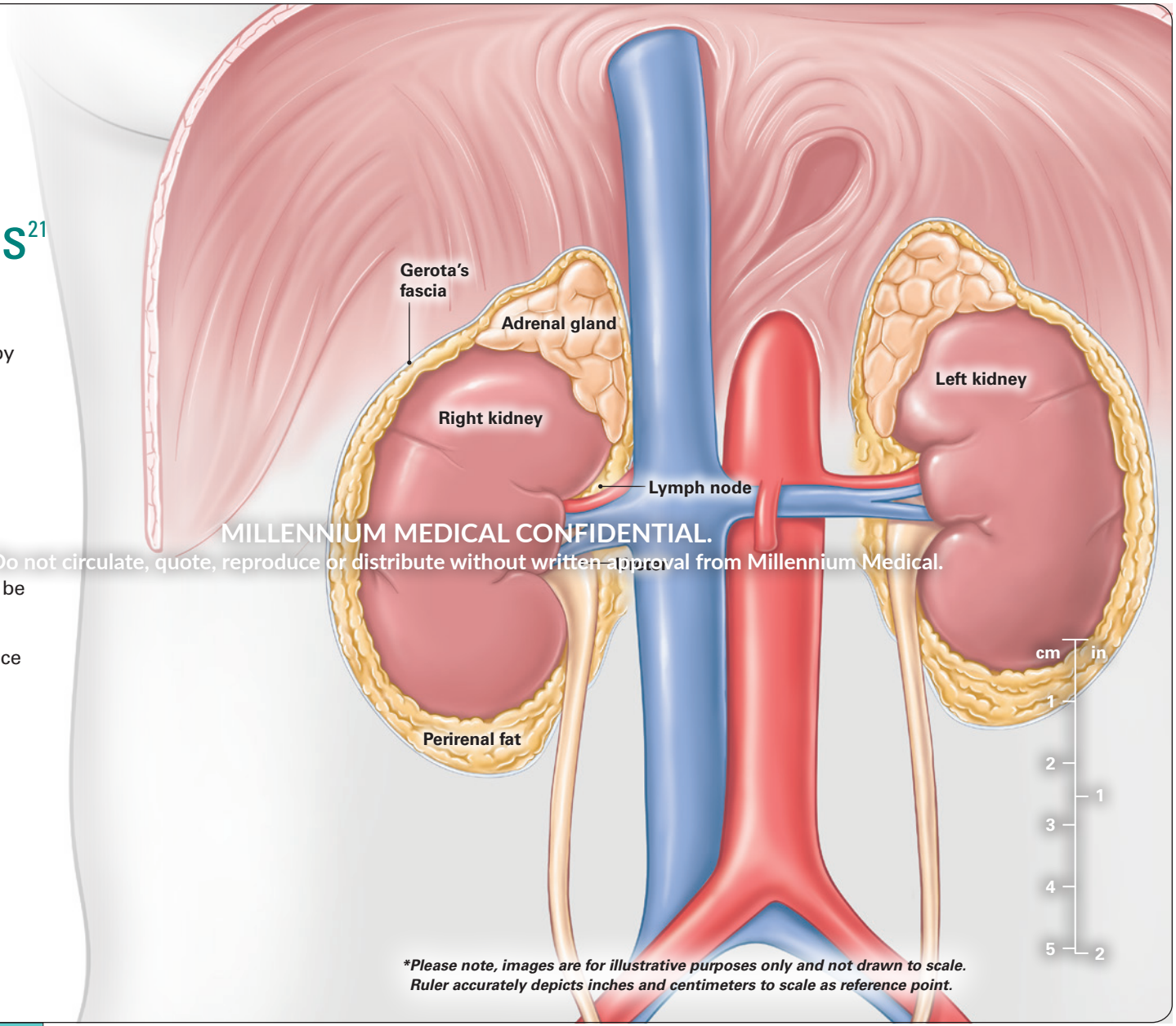

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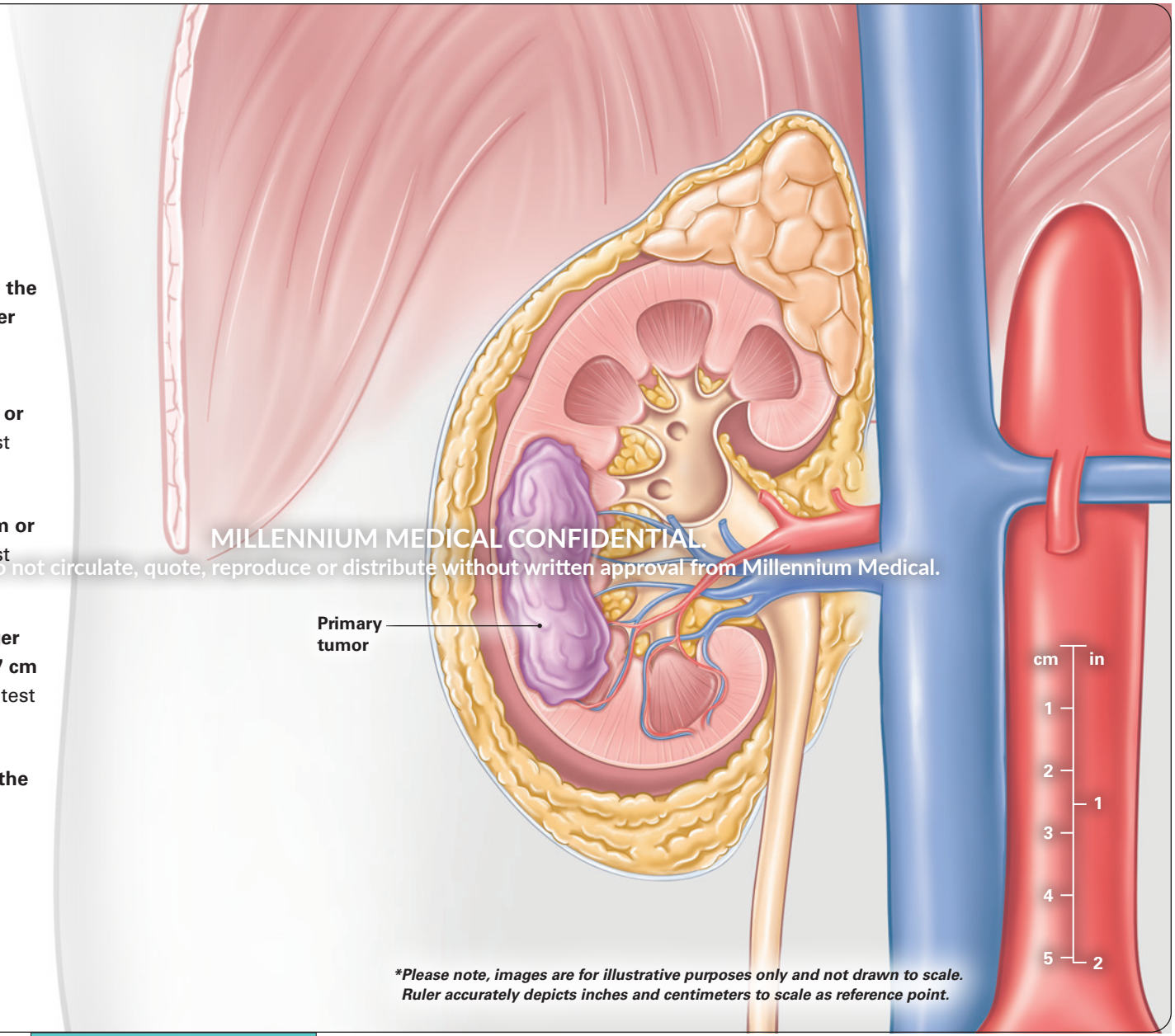
Tx, T0

Stage Tx, T0 tab

T1[21]

Tumor **is limited to the kidney** and **no larger than 7 cm**

- **T1**: Tumor is **7 cm or smaller** in greatest dimension
- **T1a**: Tumor is **4 cm or smaller** in greatest dimension
- **T1b**: Tumor **is larger than 4 cm** but is **7 cm or smaller** in greatest dimension
- **All are limited to the kidney**



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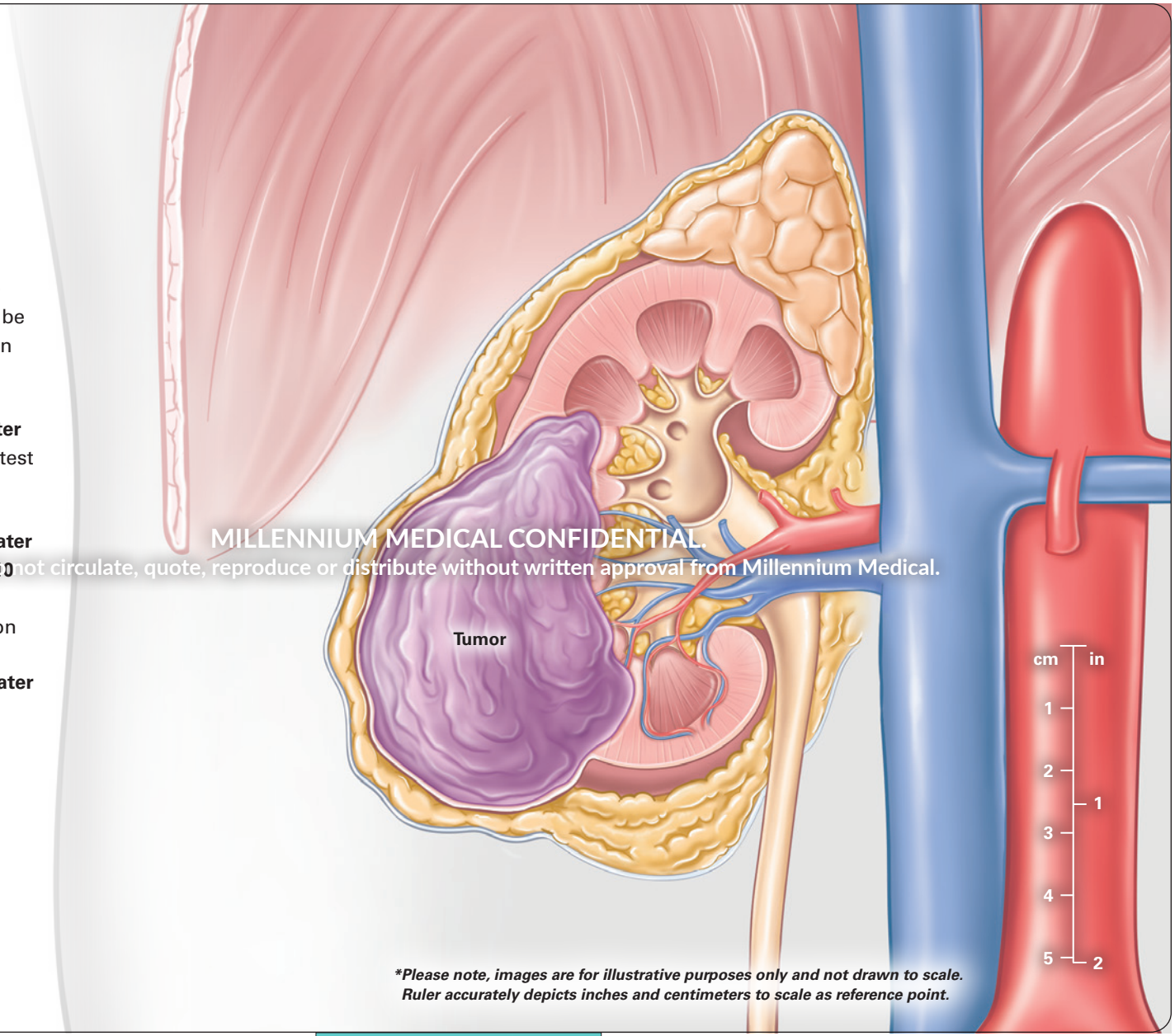
T1

Stage T1 tab

T2[21]

Tumor **is limited to the kidney** but can be **greater than 7 cm** in size

- **T2:** Tumor **is greater than 7 cm** in greatest dimension
- **T2a:** Tumor **is greater than 7 cm** but is **10 cm or smaller** in greatest dimension
- **T2b:** Tumor **is greater than 10 cm**
- **All are limited to the kidney**



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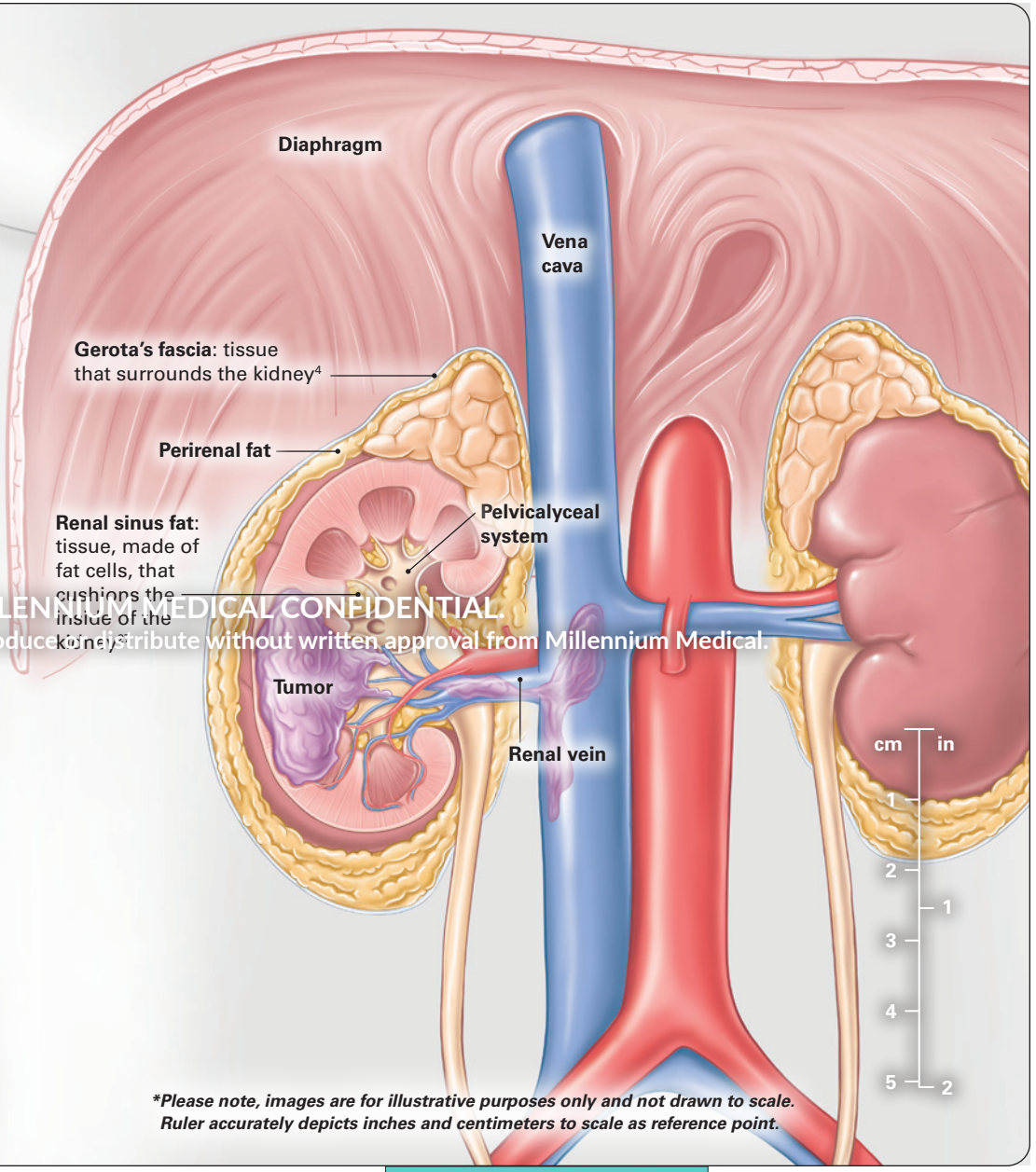
T2

Stage T2 tab

T3[21]

Tumor extends into **major veins** or **perinephric tissues,** but not into the ipsilateral adrenal gland and not beyond **Gerota's fascia**.

- **T3a:** Tumor extends into the **renal vein** or its segmental branches, or invades the **pelvicalyceal system**, or **perirenal** and/or **renal sinus fat** but not beyond Gerota's fascia
- **T3b:** Tumor extends into the **vena cava below** the **diaphragm**
- **T3c:** Tumor extends into the **vena cava above** the **diaphragm** or invades the **wall of the vena cava**
- T3 tumors are characterized by their **invasiveness into surrounding tissue, not their size**



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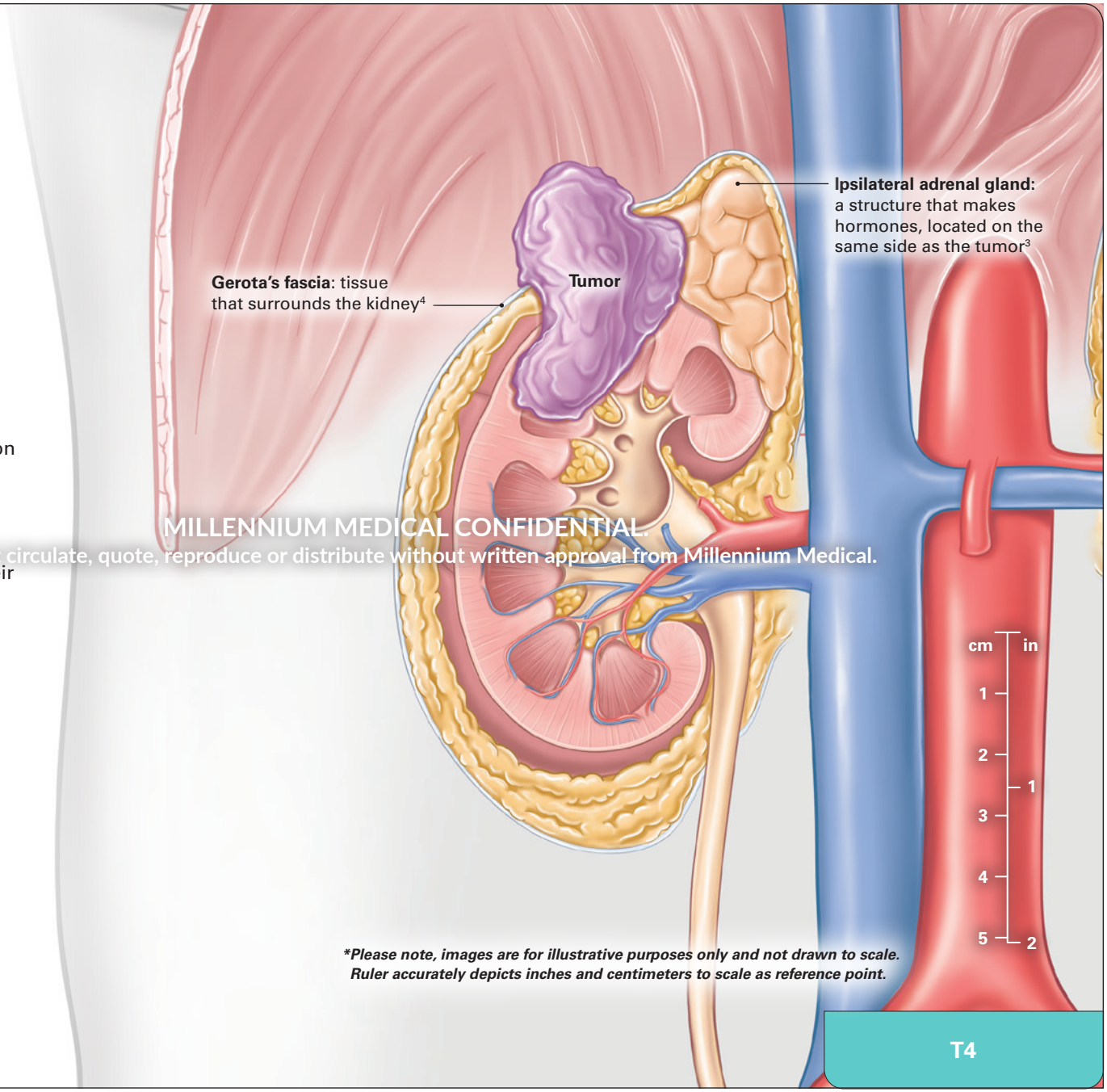
T3

Stage T3 tab

T4[21]

Tumor is beyond **Gerota's fascia**

- The tumor invades past **Gerota's fascia** (including contiguous extension into the **ipsilateral adrenal gland**)
- T4 tumors are characterized by their **invasiveness into surrounding tissue, not their size**



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Stage T4 tab

Care Team and Treatments

The healthcare providers on your care team have specialized skills and work together to treat your needs.[28]

Care team members may include[10,28,29]:

Urologist	A doctor who specializes in treating problems of the urinary tract Some may have training in oncology; these are called **Urologic Oncologists**
Medical Oncologist	A doctor who treats cancers with systemic therapy
Radiologist	A doctor trained in diagnosing diseases by reading x-rays and scans of the body
Pharmacist	A healthcare professional who specializes in safe and effective uses of medicine and treatment plans
Oncology Nurse	A nurse who has specialized training in treating and caring for patients with cancer
Pathologist	A doctor trained in diagnosing or classifying diseases from tissue or cell samples viewed under a microscope

RCC treatments may include[10,30,31]:

Surgery: a procedure that will remove the cancer tumor

Chemotherapy: the use of anti-cancer drugs

Radiation therapy: the use of high-energy rays

Systemic therapy: the use of drugs that work throughout the body

Clinical trial enrollment or **supportive care** may also be options

Every patient is unique. You and your care team will decide the best treatment plan for you.

If you have VHL disease, then you may have other specialists on your treatment team.

Primary Treatments

Primary Treatments[10,32]

Surgical removal is the primary method of treating kidney cancer. The goal of surgery is to remove all of the cancer cells, but some may remain in your body.

For some people, the chance of cancer returning after surgery (recurrence) may be higher. For patients who are at a higher risk of recurrence, treatment after surgery, called **adjuvant therapy**, may help lower the chance of recurrence.

Surgical Removal (Nephrectomy)[10]

There are two types of kidney surgeries, or nephrectomies. They depend on how much of the kidney is removed.

- **Partial:** The tumor and immediately surrounding tissue are removed. Your kidney still works after this surgery.
- **Radical**: The tumor, entire kidney, and surrounding fatty tissue are removed. Removal of the adrenal gland and nearby lymph nodes is possible. If your other kidney is healthy, it can filter enough blood for you to live a healthy life.

Additional Therapeutic Techniques[10,30]

Additional therapies may be used to treat kidney cancer.

Thermal ablation: extreme cold (cryotherapy, cryoablation) or heat used to kill cancer cells

Stereotactic Body Radiation Therapy (SBRT): used for treating brain metastases

Radiofrequency: localized radio waves used to kill cancer cells

Living with Cancer

From diagnosis to recovery, every patient's path is unique. Here are some tips to help.

It's Your Experience[10]

Get involved in your care, here's a list of questions you may have:

- What is the next step of my treatment?
- Do I need to follow a special diet during or after my treatment?
- Are there any symptoms I should watch for?

You're Not Alone

There are resources to help. Check out support groups to connect with people like you:

- National Kidney Foundation
- Kidney Cancer Coalition
- KCCure

Support Your Physical Health[33,34]

You can support your physical health through nutrition and being active:

- **Nutrition**: Maintain a kidney-friendly diet with DASH (Dietary Approaches to Stop Hypertension) and plant-based recipes
- **Exercise:** Strengthen muscles, promote healthy blood flow, and control weight

Support Your Mental Health[10]

Supporting your mental health can help your overall well-being. You can:

- **Seek help** from a professional, such as a therapist or psychologist
- **Stay connected** with family and friends by scheduling time to spend with them
- **Join a support system** to meet others like you, share your story, and be inspired

Von Hippel-Lindau (VHL) Disease-Associated RCC

What is Von Hippel-Lindau (VHL) Disease and RCC?

VHL disease is a rare (about 1 in 30,000 people) genetic condition that can cause tumors to grow in different parts of the body. It is caused by a mutation (change) in the VHL gene.[35,36,37] The VHL gene helps control cell growth, cell division, and other important functions.[38]

About 80% of people with VHL disease inherited it from a parent, while approximately 20% of people with VHL disease are a result of a random genetic mutation before birth. This is called "de novo," or "first-in-family." People who have family members with VHL disease should be tested to see if they have the mutated gene as well.[39]

How Does VHL Disease Affect the Kidneys?

People with VHL disease have a higher chance of developing a type of kidney cancer called renal cell carcinoma (RCC).[35]

About 25%–75% of people with VHL disease will develop kidney cysts or cancer.[40]

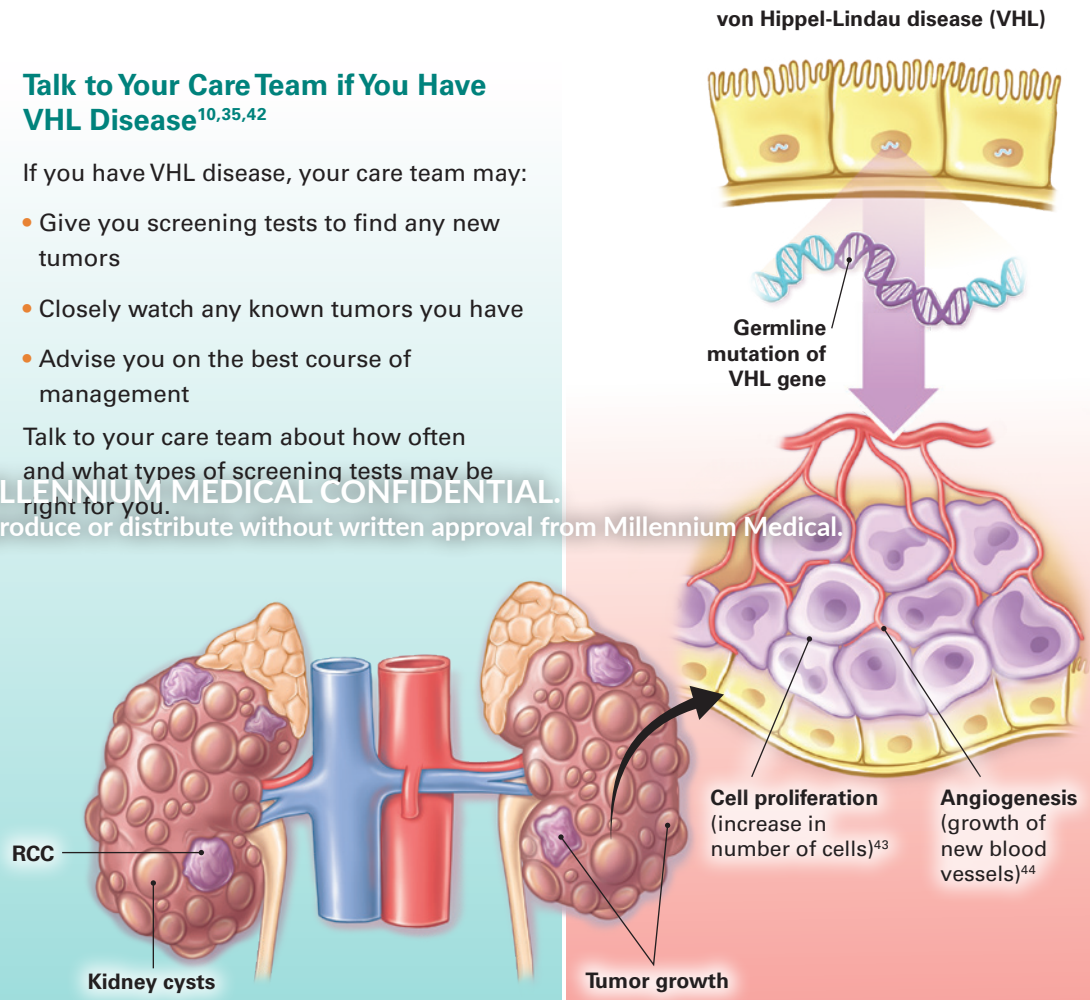
RCC can develop in people with VHL disease at a median age of **31 years old**.[41]

Talk to Your Care Team if You Have VHL Disease[10,35,42]

If you have VHL disease, your care team may:

- Give you screening tests to find any new tumors
- Closely watch any known tumors you have
- Advise you on the best course of management

Talk to your care team about how often and what types of screening tests may be right for you.



References:

1. Kidney. Stedman's Online Medical Dictionary. Accessed September 29, 2023. https://stedmansonline.com/lww/term/mlrK0900000218/659222/kidney
2. What is kidney cancer? American Cancer Society. Updated January 12, 2023. Accessed October 20, 2023. https://www.cancer.org/cancer/kidney-cancer/about/what-is-kidney-cancer.html
3. Adrenal gland. Dictionary of cancer terms. National Cancer Institute. Accessed May 7, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/adrenal-gland
4. Gerota's fascia. Dictionary of cancer terms. National Cancer Institute. Accessed May 7, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/gerotas-fascia
5. Soriano RM, Penfold D, Leslie SW. Anatomy, abdomen and pelvis: kidneys. NCBI Bookshelf. Last update July 24, 2023. Accessed September 29, 2023. https://www.ncbi.nlm.nih.gov/books/NBK482385/#_NBK482385_pubdet_
6. Kidneys. SEER Training Modules. National Cancer Institute. Accessed October 2, 2023. https://training.seer.cancer.gov/anatomy/urinary/components/kidney.html
7. Zhu W, Zheng M, Xiong S, et al. Modified Takazawa anatomical classification of renal pelvicalyceal system based on three-dimensional virtual reconstruction models. Transl Androl Urol. 2021;10(7):2944-2952. doi:10.21037/tau-21-309
8. Ureter. Dictionary of cancer terms. National Cancer Institute. Accessed September 29, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/ureter
9. Key statistics about kidney cancer. American Cancer Society. Updated January 12, 2023. Accessed May 6, 2023. https://www.cancer.org/cancer/kidney-cancer/about/key-statistics.html
10. NCCN Clinical Practice Guidelines for Patients. Kidney Cancer. Published 2024. National Comprehensive Cancer Network. https://www.nccn.org/patients/guidelines/content/PDF/kidney-patient.pdf
11. Risk factors for kidney cancer. American Cancer Society. Updated February 2023. Accessed May 5, 2023. https://www.cancer.org/cancer/kidney-cancer/causes-risks-prevention/risk-factors.html
12. Kidney cancer signs and symptoms. American Cancer Society. Updated February 1, 2020. Accessed May 5, 2023. https://www.cancer.org/cancer/kidney-cancer/detection-diagnosis-staging/signsand-symptoms.html
13. Anemia. Dictionary of cancer terms. National Cancer Institute. Accessed May 5, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/anemia
14. New Prognostic Model More Accurately Predicts Kidney Cancer Recurrence and Survival. Fox Chase Cancer Center. January 10, 2022. Accessed October 24, 2023. https://www.foxchase.org/news/2021-06-08-new-prognostic-model-more-accurately-predicts-kidney-cancer-recurrence-and-patient-survival
15. Tests for kidney cancer. American Cancer Society. Published online February 1, 2020. Accessed May 5, 2023. https://www.cancer.org/cancer/kidney-cancer/detection-diagnosis-staging/how-diagnosed.html
16. CT scan. Dictionary of cancer terms. National Cancer Institute. Accessed May 5, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/ct-scan
17. MRI. Dictionary of cancer terms. National Cancer Institute. Accessed May 5, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/mri
18. Ultrasound. Dictionary of cancer terms. National Cancer Institute. Accessed May 5, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/ultrasound
19. Angiography. Dictionary of cancer terms. National Cancer Institute. Accessed September 25, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/angiography
20. Wahal SP, Mardi K. Multilocular cystic renal cell carcinoma: a rare entity with review of literature. *J Lab Physicians.* 2014;6(1):50-52. doi:10.4103/0974-2727.129093
21. Amin MB, Edge SB. In: AJCC Cancer Staging Manual. 8th ed. Berlin. Springer; 2017.
22. Tumor Grade. Dictionary of cancer terms. National Cancer Institute. Accessed September 29, 2023. https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-grade
23. Warren AY, Harrison D. WHO/ISUP classification, grading and pathological staging of renal cell carcinoma: standards and controversies. *World J Urol.* 2018;36(12):1913-1926. doi: 10.1007/s00345-018-2447-8
24. Molecular testing. Dictionary of cancer terms. National Cancer Institute. Accessed May 6, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/molecular-testing
25. Surrogate endpoint. Dictionary of cancer terms. National Cancer Institute. Accessed May 5, 2023. https://www.cancer.gov/publications/dictionaries/cancerterms/def/surrogate-endpoint
26. Khalid N, Azimpouran M. Necrosis. NCBI Bookshelf. Updated March 6, 2023. Accessed September 29, 2023. https://www.ncbi.nlm.nih.gov/books/NBK557627/
27. Renal sinus. Cleveland Clinic. Updated September 14, 2022. Accessed May 7, 2023. https://my.clevelandclinic.org/health/
28. Health professionals associated with cancer care. American Cancer Society. Updated August 7, 2019. Accessed May 5, 2023. https://www.cancer.org/treatment/treatments-and-side-effects/choosing-your-treatment-team/health-professionals-associated-withcancer-care.html
29. Oncology nurse. National Cancer Institute. Accessed May 5, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/oncology-nurse
30. Treatment of kidney cancer by stage. American Cancer Society. Updated November 22, 2021. Accessed May 5, 2023. https://www.cancer.org/cancer/kidney-cancer/treating/by-stage.html
31. Chemotherapy. Stedman's Online Medical Dictionary. Accessed October 1, 2023. https://stedmansonline.com/lww/term/mlrK0900000218/659222/chemotherapy
32. Adjuvant therapy. Dictionary of Cancer Terms. National Cancer Institute. Accessed November 16, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/adjuvant-therapy
33. The DASH diet. National Kidney Foundation. Accessed September 28, 2023. https://www.kidney.org/atoz/content/Dash_Diet
34. Exercise: What you should know. National Kidney Foundation. Reviewed March 2014. Accessed September 28, 2023. https://www.kidney.org/atoz/content/exercisewyska
35. Von Hippel-Lindau syndrome. Cancer.net. Updated September 2021. Accessed September 28, 2023. https://www.cancer.net/cancer-types/von-hippel-lindau-syndrome
36. Rare diseases at FDA. Food and Drug Administration. Content current as of December 13, 2022. Accessed November 16, 2023. https://www.fda.gov/patients/rare-diseases-fda
37. Von Hippel-Lindau Disease. National Organization for Rare Diseases. Last updated October 25, 2023. Accessed November 16, 2023. https://rarediseases.org/rare-diseases/von-hippel-lindau-disease/?filter=ovr-ds-resources#completereport
38. VHL gene. Dictionary of cancer terms. National Cancer Institute. Accessed September 28, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/vhl-gene
39. van Leeuwaarde RS, Ahmad S, Links TP, et al. Von Hippel-Lindau Syndrome. In: Adam MP, Mirzaa GM, Pagon RA, et al., GeneReviews [Internet]: 2000 May 17 [Updated 2018 Sep 6]. https://www.ncbi.nlm.nih.gov/books/NBK1463/
40. Rednam SP, Erez A, Druker H, et al. Von Hippel-Lindau and hereditary pheochromocytoma/paraganglioma syndromes: clinical features, genetics, and surveillance recommendations in childhood. Clin Cancer Res. 2017;23(12):e68-e75. doi:10.1158/1078-0432.CCR-17-0547
41. Feletti A, Anglani M, Scarpa B, et al. Von Hippel-Lindau disease: an evaluation of natural history and functional disability. Neuro Oncol. 2016;18(7):1011-1020. doi:10.1093/neuonc/nov313
42. What you need to know about VHL: a reference handbook for people with von Hippel-Lindau, their families, and their medical teams. 6th Ed. VHL Alliance. Revised 2020. Accessed October 3, 2023. https://www.vhl.org/wp-content/uploads/2022/12/vhla-handbook-2020.pdf
43. Cell Proliferation. Dictionary of cancer terms. National Cancer Institute. Accessed September 22, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cell-proliferation
44. Angiogenesis. Dictionary of cancer terms. National Cancer Institute. Accessed September 29, 2023. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/angiogenesis

TENT CARD