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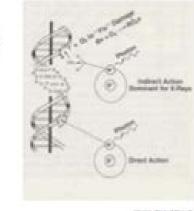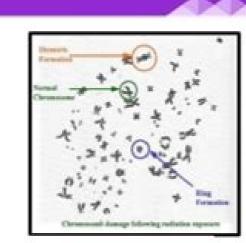
### Table 4: Summary of Radiomic Feature Classes

| Feature Class | Examples | Note |
|---|---|---|
| Morphologic | Diameter, area, sphericity | Semantic features may represent descriptive scores (eg, small, medium, large). However, there are corresponding morphologic radiomic features that are purely quantitative. |
| Intensity | Minimum, maximum, mean 10th and 90th percentiles, skewness, kurtosis | First-order features describe properties of the distribution of SIs within an ROI (eg, the minimum, maximum, mean, median, range, standard deviation, and 10th and 90th percentiles of the intensities). Skewness refers to asymmetry of the distribution of values about the mean and can be positive or negative. Kurtosis refers to the tail behavior of the SI distribution, with higher values implying a higher proportion of SI values concentrated toward the tails and a lower proportion toward the mean. |
| Texture features | Contrast, correlation, entropy, run emphasis, gray-level nonuniformity | Second-order features describe spatial complexity and relationships of SIs between neighboring pixels; often computed from the co-occurrence matrix (GLCM) described by Haralick (8) or the run-length matrix (GLRLM) described by Galloway (29). Other classes include those derived from the gray-level size-zone matrix (GLSZM) (30), gray-level distance-zone matrix (GLDZM) (30), neighborhood gray-tone difference matrix (NGTDM) (31), and neighborhood gray-level dependence matrix (NGLDM) (32). |



## 2.2 Radiation Chemistry

- **Indirect action:** Electrons produce free radicals which break chemical bonds and produce chemical changes

- **Direct Action:** Photon ejects an electron which produce a biological damage on the DNA

**Drug Delivery:**

Polymers such as thermosensitive polymers are now finding applications in drug delivery system development. Radiotracers have been used for the evaluation and determination of efficiency and target evaluation of these novel drug delivery systems. These polymers based drug delivery systems can be used for radiotherapy.

**Radioimmunoassay:**

Radioimmunoassay is yet another application of the radiotracer. Since development of Radioimmunoassay (RIA), variety of immunoassays and their variants have been developed in clinical, analytical and research laboratories for the detection and quantification of molecules in very minute quantities. Apart from the precise measurement they have provided an insight into basic mechanism and revolutionized our understanding of many physiological and pathological phenomenon.

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## Review Questions

- What are the faults of radioimmunoassay testing?
- Why is the test still used despite its faults?
- What can radioimmunoassay be used for?
- How much of a substance can RIA testing measure per milliliter of blood?
  - One trillionth of a gram
- Does the RIA test require a confirmatory test along with it?

The well is again washed. The radiolabelled antigen is then added. The EIA was developed by Van Weemen and Schuurs (independently of Engvail and Perlman) for the quantification of antigen rather than antibody. This proves problematic when the antigen of interest is in low abundance as the sensitivity of the test is reduced. Secondary antibodies can therefore be made commercially available at a much lower price, and with a variety of signal-producing conjugates (i.e. all ELISAs using a rabbit-derived primary antibody could use the same anti-rabbit IgG secondary antibody).The direct and indirect methods both suffer from the fact that complex samples will reduce the sensitivity of the experiment due to a variety of proteins adsorbing to the well. The enzyme is designed so as to become deactivated by antibody binding. Analyte samples in biological specimens should lie on the straight part of the curve.There are a variety of ELISA methods. These assays include competition assays using fluorescent peptides, and also a variety of (g) Actual standard curve for urotensin-II (UII) where amount of radioactive iodine bound is expressed as B/B0 which is the ratio of binding at each standard concentration, B to that bound in the absence of displacer, B0. The antigen and the biotinylated antigen will compete for the same site on the antibody. If both capture and primary antibody were from the same species, then the secondary antibody would bind to both and not reflect differences in bound antigen.This method requires two ligands to compete with each other for a limited number of antibody sites. (e) Actual standard curve for a sandwich TNF-α assay. Bound and unbound fluorescein-conjugated antigens emit fluorescence of different intensities and can therefore be distinguished. For the purpose of this article, EIA and ELISA should be considered interchangeable.The majority of RIA assay formats recommend sample cleaning and concentration (particularly when analyte concentration and assay sensitivity is low), although a large number of ELISA assays can cope with direct use of unprocessed plasma. The important variations are described below (Fig. 2).Fig 2Schematic showing the differences between direct (a), indirect (b), sandwich (c), and competitive (d) EIA methods. A second antibody that binds the primary antibody can then be added, along with serum from the species of the primary antibody, to cause the solution to flocculate and allow for separation of the primary antibody from solution. The sandwich method overcomes this. In complex samples, containing a range of different proteins, there will be a variety of proteins adsorbed onto the well that are not the antigen of interest. This method is the enzyme-linked immunosorbent assay (ELISA). 2012; 109: 345-351Effect of preoperative fever-range whole-body hyperthermia on immunological markers in patients undergoing colorectal cancer surgery.Br J Anaesth. Published by Elsevier Inc. Remaining binding sites on the well are then blocked. A complimentary antibody (primary antibody) is then added, which binds to the antigen forming a complex. This is often achieved by adding biotin to the antigen of interest. 2006; 12: 4716-4720View in Article Scopus (12) PubMed Crossref Google ScholarNeither nociceptin nor its receptor are present in human synovial fluid or tissue.Br J Anaesth. 2011; 107: 612-618Handling editor: R. The wells are then washed thoroughly, leaving only the absorbed antigen. 1984; 30: 200-205View in Article Tech tip #65: ELISA technical guide and protocols, Available from in Article Influence of confounding factors on plasma mid-regional pro-adrenomedullin and mid-regional pro-A-type natriuretic peptide concentrations in healthy individuals.Biomarkers. 1971; 8: 871-874View in Article Scopus (2770) PubMed Crossref Google ScholarImmunoassay using antigen-enzyme conjugates.FEBS Lett. The first immunoassay developed was described by Yalow and Berson in 1959. This method differs from the direct method in that the antibody binding to the antigen does not have attached to it an enzyme or any other signal-generating substance. RLU, relative light units signal from the enzyme reaction.This is the simplest of the ELISA techniques. 2011; 16: 281-287View in Article Scopus (15) PubMed Crossref Google ScholarFluoroimmunoassays and immunofluorometric assays.Clin Chem. Other assays, such as Enzyme multiplied immunoassay technique (EMIT)17Schneider RS Lindquist P Wong ET Rubenstein KE Ullman EF Homogeneous enzyme immunoassay for opiates in urine. MahajanDOI: ❖ 2014 The Author(s). The signal generated by this assay will be inversely proportional to the amount of antigen in the sample.As mentioned, biotin is often added to the competing antigen. It also binds readily and specifically to streptavidin. Analyte samples in biological specimens should lie on the straight part of the curve. The sample will contain the antigen of interest. 2004; 25: 1339-1347View in Article Scopus (18) PubMed Crossref Google ScholarThe nociceptin/orphanin FQ receptor: a target with broad therapeutic potential.Nat Rev Drug Discov. Streptavidin is a protein that is easily conjugated to a variety of molecules, allowing signal generation from a variety of sources such as colour changes, chemiluminescence (immunoluminometric assay),15Bhandari SS Davies JE Struck J Ng LL Influence of confounding factors on plasma mid-regional pro-adrenomedullin and mid-regional pro-A-type natriuretic peptide concentrations in healthy individuals.Crossref PubMed Scopus (15) Google Scholar and fluorescence (immunofluorometric assay). A blocking agent is added as before and a sample is then added. This allows labelled streptavidin compounds for use with biotinylated antibodies or peptides.The above assay formats are heterogeneous immunoassays (assays that require separation of bound and unbound antibody/antigen before signal recording). 2008; 7: 694-710View in Article Scopus (274) PubMed Crossref Google ScholarEditorial III: Nociceptin/orphanin FQ peptide-receptor system: are we any nearer the clinic?.Br J Anaesth. Note the way the standard curve is presented varies with the RIA in Figure 1, but analyte samples in biological specimens should lie on the straight part of the curve. The sample will contain the antigen of interest. multiple secondary antibodies to bind to the same primary antibody, thereby amplifying the signal and increasing the sensitivity of the test (although there is still the issue of complex samples having multiple proteins adsorbed onto the surface of the well).Another advantage of this method is the exclusion of the need to conjugate the primary antibody, avoiding the problems described above. Enzymes are, however, open to interference. The more sample antigen present, the less the radiolabelled antigen is able to bind to the antibody. (b) Radiolabelled peptide is then added. (c) Secondary antibody binds to primary antibody and causes it to precipitate out of solution. The drawbacks of RIA relate to the use of a radiolabel (usually [125I]) and hence short shelf life. 2000; 22: 71-76View in Article Scopus (43) PubMed Crossref Google ScholarRelative concentrations of haemostatic factors and cytokines in solvent/detergent-treated and fresh-frozen plasma.Br J Anaesth. and Fluorescence polarization immunoassays (FPIA) do not require this separation, and are classified as homogenous immunoassays. Elsevier user license | How you can reuse Permitted For non-commercial purposes: Read, print & download Text & data mine Translate the article Not Permitted Reuse portions or extracts from the article in other works Redistribute or republish the final article Sell or re-use for commercial purposes Elsevier's open access license policy Access this article on ScienceDirect In 1971, Engvail and Perlman described a technique whereby antigens were immobilized on a microplate well, incubated with antiserum, and then the concentration of antibody in the antiserum was quantified using an enzyme-linked anti-immunoglobulin antibody. This is particularly important in anaesthesia, intensive care, and pain research for the quantification of mediators (cytokines, peptides, and analytes) involved in inflammation, pain, and other pathways.Immunoassays use the high specificity of antibodies, along with their enormous diversity, to target specific molecules of interest and analyse their concentration in a sample. The radiolabelled antigen competes with the sample antigen and displaces it from the antibody. FPIA works similarly, with fluorescein-conjugated antigens competing. (f) Example of a typical standard curve. They used radiolabelled insulin to assess the concentration of insulin in human plasma, and thus developed the first radioimmunoassay (RIA). 2011; 106: 505-511Blockade of spinal nerves inhibits expression of neural growth factor in the myocardium at an early stage of acute myocardial infarction in rats.Br J Anaesth. P. This costly and time-consuming process has to be repeated for each individual ELISA, a problem avoided by the other methods. It does, however, have some limitations. 2012; 109: 754-761Effectiveness of electroacupuncture analgesia compared with opioid administration in a dog model: A pilot study.Br J Anaesth. Another issue is that the antibody needs to have an enzyme attached to it. If a secondary antibody is used (as in indirect ELISA), it is important that the capture and primary antibodies are raised in different species. This can result from specificity of the antibody (e.g. the cardiovascular peptide urotensin II) or the fluid in which the analyte is suspended interfering with only one type of assay (e.g. the opioid-related peptide Nociceptin/Orphanin FQ).. , , . Discordance has also been demonstrated between RIAs and EIAs measuring cortisol and carcinoembryonic antigen. 1959; 184: 1648-1649View in Article Scopus (704) PubMed Crossref Google ScholarIt's about the journey, not the destination: the birth of radioimmunoassay. It does however come at a cost. Quantitative assay of immunoglobulin G.Immunochemistry. Enzyme immunoassays (EIAs) are very similar to ELISAs, and as such, the terms are often used interchangeably. By measuring the radioactivity of the pellet, it is possible to determine the amount of radiolabelled antigen that has bound to antibody, and therefore the concentration of antigen in the sample (Fig. 1). Also, conjugating the antibody with an enzyme has the potential to reduce the affinity of the antibody to the antigen, and thus reduce sensitivity once more.Sample containing the antigen of interest is adsorbed onto the wells of a microplate, followed by blocking of remaining sites on the well. 1973; 19: 821-825View in Article Fluorescence polarization immunoassay: detection of antibody to brucella abortus.Methods. It is a useful molecule since it is small, and thus does not appreciably reduce the affinity of the antigen for the antibody. For this method to work, two antigen-specific antibodies are required. 1985; 31: 359-370View in Article Homogeneous enzyme immunoassay for opiates in urine.Clin Chem. The sample antigen and antibody are incubated together, allowing the sample antigen to bind with the antibody. An antibody complementary to that of the antigen (capture antibody) is first added to the plate where it is adsorbed to the well. (d) Centrifugation causes the antibody-antigen complex to form a pellet. 1960.Clin Chem. These assays do not use enzymes and thus reduces the risk of interference from the sample itself.Fig 1(a) Sample peptide is incubated with primary antibody. 13Fleisher M Nisselbaum JS Loftin L Smith C Schwartz MK Roche RIA and Abbott EIA carcinoembryonic antigen assays compared. We would recommend users to determine if sample cleaning is required for their analyte.Often, there are differences in measured analyte concentration when comparing RIA and ELISA. One ligand will be the antigen of interest, and one will be a similar molecule that is able to bind to the antibody, but has a variation that allows a further molecule to exclusively bind to it. Detection may be based on colour, fluorescence, or luminescence.This method has the advantage of being quicker and simpler than the other ELISA methods, with fewer steps, and just one antibody. EMIT requires an enzyme-linked antigen that will compete with sample antigen for antibody binding. The cleaning and concentration process usually involves ion exchange chromatography followed by some form of freeze drying/lyophilization. The biotin-streptavidin complex can also be used as a signal amplifier.The use of enzymes in an assay can be advantageous since this allows for the use of a variety of substrates that can generate different signals. 2007; 21: 378-389View in Article Scopus (39) PubMed Crossref Google ScholarDifferential levels of 'urotensin-II-like' activity determined by radio-receptor and radioimmuno-assays.Peptides. This secondary antibody will have been raised in an animal different from that of the origin of the primary antibody and will target the Fc region of the primary antibody. The secondary antibody is often polyclonal (originates from different B cells) and as such will be responsive to different epitopes on the primary antibody. The ability to quantify the amount of a specific protein in a complex sample has been a valuable addition to laboratory science, allowing the development of diagnostic tests, allergen detection in the food industry, and screening for immunity. 1999; 83: 470-471View in Article Scopus (16) PubMed Abstract Full Text PDF Google ScholarNociceptin and urotensin-II concentrations in critically ill patients with sepsis.Br J Anaesth. The sample is first added to the microplate well and incubated. This leaves a bound antigen-antibody complex on the surface of the well. Only the antigen of interest can remain on the plate since it is able to bind to the antibody. Some recent British Journal of Anaesthesia RIA/ELISA data are summarized in Table 1.D.G.L. holds a consultancy with Grunenthal GmbH, but this is not directly related to the content of this article. It competes with sample peptide and displaces it. Since solution containing antigen-antibody complex is more dense than that containing free-antigen, centrifuging this mixture allows separation, resulting in a pellet containing the bound sample antigen/radiolabelled antigen. 2002; 48: 207-208View in Article Roche RIA and Abbott EIA carcinoembryonic antigen assays compared.Clin Chem. For example, horseradish peroxidase and alkaline phosphatase are the most frequently used enzymes and are inhibited by buffers containing sodium azide (a commonly used preservative) and phosphate, respectively. The selection of assay format is therefore critical and the remainder of this article covers the main formats currently available.An RIA requires the following: a sample containing the antigen of interest, a complementary antibody, and a radiolabelled version of the antigen. A substrate is then added which will be converted by the enzyme into a detectable product. 2008; 100: 810-814Comparison of two methods for measuring salivary cortisol.Clin Chem. The rest of the experiment can now proceed in the same way as a direct or an indirect ELISA. The clear benefit of this method is improved sensitivity. This is because the secondary antibody will be raised against the species of the primary antibody. Instead, the purpose of this antibody is to act as a bridge between the antigen and a secondary (enzyme-linked) antibody. D.G.L. is the administration director and a board member of BJA, and J.P.T. is an editor and board member of BJA.Assay of plasma insulin in human subjects by immunological methods.Nature. 2004; 93: 626-628Low utility of plasma Nociceptin/orphanin FQ in the diagnosis of hepatocellular carcinoma.World J Gastroenterol. The bound antibody will have attached to it an enzyme. The antigen becomes adsorbed onto the surface of the well. 2010; 56: 671-672View in Article Scopus (4) PubMed Crossref Google ScholarEnzyme-linked immunosorbent assay (ELISA). They need to bind to different epitopes on the antigen, and these need to be far enough away from each other as to not hinder the binding of one another. An antibody, complementary to the antigen of interest, is then added to the wells where it binds to the antigen. 1971; 15: 232-236View in Article Scopus (669) PubMed Crossref Google ScholarRole of urotensin II and its receptor in health and disease.J Anesth. Endogenous sample peroxidases and phosphates may also interfere with the assay.Immunoassays that do not require the use of enzymes and radionuclides are now being developed.

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