are considered, and depending on which indicator of each dimension is used. The effects of treatment modalities are not the same, or not even in the same rank order, for all the different dimensions of breast cancer. Clinical trials and other research—and, therefore, the preferences between treatments—are mainly based on the biological dimension. However, other dimensions should also affect treatment policies.

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Patterns of Metastatic Breast Cancer in Relation to Histological Type

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We have examined the clinical records of 1238 patients with operable breast cancer to identify the sites of metastatic disease. Infiltrating ductal carcinoma (IDC) recurred more commonly in lung ($P < 0.05$), pleura ($P < 0.05$) and brain ($P < 0.05$), while infiltrating lobular carcinoma (ILC) more commonly metastasised to the bone marrow ($P < 0.01$) and peritoneum ($P < 0.01$). Bone involvement as the initial presentation of distant metastatic disease occurred in over 50% of women with ILC, significantly more commonly than in those with IDC (34%, $P < 0.01$). Survival was similar for the two groups, both from time of diagnosis and from time of development of distant metastases.
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INTRODUCTION

THE TWO main histological variants of infiltrating breast cancer, infiltrating ductal carcinoma (IDC) (70–80% of cases) and infiltrating lobular carcinoma (ILC) (10–14%) [1, 2], have been reported to show different patterns of metastatic spread [3–6]. Recurrence in the meninges, bone marrow and peritoneum is more common in ILC and recurrence in the lung in IDC.

Differences in survival after development of metastases have also been noted, patients with ILC faring significantly better than those with IDC [5, 6]. As such differences could be of importance in patient management we reviewed our data to confirm these findings.

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PATIENTS AND METHODS

Patients

Between 1977 and 1986, 1391 patients with primary operable invasive breast cancer were treated at Guy's Hospital Breast Unit and histological diagnoses were performed using established criteria [7]. IDC (including mixed tubular pattern) was diagnosed in 1069 cases (76%) and ILC (classical and variant) in 177 cases (13%). Other histological types were not included in the analysis.

Clinical information

Clinical records were examined and the sites and dates of tumour recurrence noted. Bone metastases were differentiated according to whether they involved the calcified matrix, referred to as 'bone' (diagnosed radiographically) or the bone marrow (diagnosed cytologically). Peritoneal involvement was diagnosed by imaging, laparotomy, or deduced from the presence of

Table 1. Patients' characteristics at presentation

	IDC (n = 1060)	ILC (n = 177)	P
Age (years)			0.02
Mean	54.3	56.3	
Range	20–98	32–86	
Menopausal status			
Pre	428 (40%)	64 (36%)	
Peri	130 (12%)	18 (10%)	NS
Post	483 (46%)	92 (52%)	
Uncertain	19 (2%)	3 (2%)	
Tumour size (cm)			
Mean	2.92	3.18	0.02
Range	0–10	0–9	
No. of axillary lymph nodes involved			
0	515 (49%)	93 (53%)	
1–3	341 (32%)	46 (26%)	NS
> 4	204 (19%)	38 (21%)	
Oestrogen receptor status			
≤ 10 fmol/mg cytosol protein	246 (23%)	34 (19%)	
> 10 fmol/mg cytosol protein	714 (67%)	121 (68%)	NS
Unknown	100 (9%)	22 (12%)	
Progesterone receptor status			
≤ 10 fmol/mg cytosol protein	427 (40%)	65 (37%)	
> 10 fmol/mg cytosol protein	500 (47%)	86 (49%)	NS
Unknown	133 (12%)	26 (15%)	

NS, non-significant.

malignant cells in ascitic fluid in the absence of gross abdominal visceral involvement. All patients had regular follow-up.

Statistical analysis

Fisher's exact test was used to determine statistical differences between sites of metastases. Survival was compared using the method of Kaplan and Meier [8], with significance being determined using the log rank test. Survival data was analysed using the SUREAL package. A result was considered statistically significant if $P < 0.05$, and otherwise non-significant (NS).

RESULTS

The patients with ILC were, on average, older than those with IDC and had significantly larger tumours (Table 1). The two groups were similar with regard to menopausal status, lymph node involvement and receptor status. Methods of treatment were similar. 92 (9%) patients with IDC and 23 (13%) patients with ILC developed contralateral breast cancer (NS). Local recurrence occurred in 246 (23%) patients with IDC and 43 (24%) with ILC (NS). Distant metastases occurred in 397 (37%) patients with IDC and 63 (35%) with ILC (NS) (Table 2). IDC metastasised significantly more commonly to the lungs ($P < 0.05$), pleura ($P < 0.05$) and brain ($P < 0.05$), whereas ILC more commonly metastasised to bone marrow ($P < 0.01$) and the peritoneum ($P < 0.01$). Meningeal involvement was rare.

First distant recurrence in bone was significantly more fre-

Table 2. Metastatic patterns and sites of first distant recurrences of IDC and ILC

	Number of patients IDC (n = 397)	ILC (n = 63)	P
Metastatic pattern of IDC and ILC			
Soft tissue	256 (65%)	31 (49%)	NS
Bone	276 (70%)	48 (76%)	NS
Bone marrow	20 (5%)	9 (15%)	0.009
Lung	123 (31%)	10 (16%)	0.02
Pleura	136 (34%)	13 (21%)	0.04
Liver	140 (35%)	19 (31%)	NS
Brain	44 (11%)	1 (2%)	0.02
Meninges	7 (2%)	2 (3%)	NS
Pericardium	12 (3%)	0	NS
Mediastinum	17 (4%)	1 (2%)	NS
Peritoneum	11 (3%)	7 (11%)	0.006
Sites of first distant recurrence of IDC and ILC			
Soft tissue	70 (18%)	8 (13%)	NS
Bone	135 (34%)	33 (52%)	0.007
Lung	48 (12%)	2 (3%)	0.04
Pleura	53 (13%)	5 (8%)	NS
Liver	34 (9%)	4 (6%)	NS
Bone marrow	3 (1%)	1 (2%)	NS
Brain	10 (3%)	1 (2%)	NS

quent for patients with ILC ($P < 0.01$) and in lung for those with IDC ($P < 0.05$).

Survival from diagnosis, distant metastatic-free interval and survival after development of distant metastases, were similar for the two histological groups.

DISCUSSION

IDC and ILC of the breast have distinct histological patterns, and significant differences in their clinical behaviour have been suggested. There are conflicting reports regarding differences in survival [6, 9, 10]. ILC has been reported to metastasise more commonly to meninges, bone marrow, peritoneum and liver, and IDC more commonly to the lungs [3, 5]. Interestingly, studies of autopsy material have revealed substantial metastatic spread that had remained clinically undetected [3, 4], especially with involvement of the peritoneum and abdominal organs in patients with ILC, when the metastases had a distinctive, diffuse pattern. Although examination of autopsy data from our unit provided insufficient information for full analysis, 3 of 4 patients with ILC had peritoneal metastases compared with only 3 of 52 patients with IDC.

In general, our findings agree with previous reports, confirming that ILC metastasises more frequently to bone marrow ($P < 0.01$) and peritoneum ($P < 0.01$) and that IDC is more likely to spread to the lungs ($P < 0.05$), brain parenchyma ($P < 0.05$) and pleura ($P < 0.05$). Harris *et al.* [3] reported a striking propensity for meningeal involvement in patients with ILC but, in our study, meningeal metastases were rare, occurring in only 2% of all patients with distant metastatic spread [3, 5, 6].

As disease progresses, metastases usually involve more than one site and in the terminal stages widespread dissemination is common [11] and may explain differences in clinical and autopsy findings. This suggests that, unless timing of recurrence is analysed, as well as site, data may not accurately reflect clinical behaviour. Attention to the site of first distant recurrence addresses this difficulty. In our series, over half of the patients with ILC who developed distant metastases presented first with bone recurrence, compared with a third of those with IDC. Previous reports have shown bone involvement to be the first site of distant metastasis in 24–47% of cases of breast cancer [12–14], but have not considered histologically different types of primary carcinoma. As bone metastases are an important cause of morbidity, resulting in pathological fractures and hypercalcaemia, their early detection in specific risk groups may be important. Treatment regimens to reduce complications may be more effective the earlier they are initiated [15].

Follow-up showed that the two groups had similar survival, both from time of diagnosis and time of development of distant metastases. Two studies from the same centre [5, 6] have shown a slight survival advantage for patients with ILC over those with IDC after development of distant metastases. One reason for different prognostic findings in the literature [6, 9, 10] may be because of changes in criteria for classifying breast cancer. ILC and its variants are now better recognised, and consequently numbers in the ILC category have increased. Secondly, more specialised types of IDC are also recognised now and separated from the non-specialised (NOS) ductal group. In a recent report showing ILC to have a significant survival advantage over IDC [10], tubular mixed carcinomas were excluded, along with other subtypes with a favourable prognosis, from the ductal NOS group.

This study has demonstrated definite differences in the metastatic patterns of IDC and ILC. In particular, ILC has a greater propensity to metastasise to bone marrow, and for its first site of distant recurrence to be bone. Further detailed studies, relating the time course of metastatic spread in breast cancer to prognosis, may be of additional value. This, together with improvements in the classification of breast cancer by both histological and molecular methods, is likely to enhance our understanding of its behaviour.

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